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THE THALAMIC AND PARKINSONIAN TYPES OF INFUNDIBULAR TUMORS

THE OCCURRENCE OF GLYCOREGULATORY AND SO-CALLED ENDOCRINE DISORDERS *

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The fundamental work on infundibular tumors was that of Weisenburg,[1] in 1910, which detailed thirty cases that had been completely studied. In his second case was the first description of a thalamic type of infundibular tumor; the author noted pain of the central type and vasomotor or trophic disturbances on the opposite side, these symptoms being due to direct destruction of the thalamus by the neoplasm. This is an exceptional case, as evidenced by the fact that in three of the thirty cases reported the thalamus was compressed without giving rise to specific clinical symptoms. Weisenburg also cited a case of Barié in which anesthesia of both extremities was present.

Other extrapyramidal symptoms—tremor, involuntary rhythmic movements, states of rigidity, fits, bradylalia, facial rigidity and slowness of gait—have been reported by Berger-Erdheim,[2] Bregmann-Steinhaus,[3] Russell,[4] Claude and Schaeffer,[5] Thomas, Jumentié and Chausseblanche,[6] Sainton and Peron [7] and Cuel,[8] but these phenomena usually appeared separately and were often transitory.

* From the Pathological Institute of the University of Brussels, Prof. A. P. Dustin.

1. Weisenburg, T. H.: Tumors of the Third Ventricle, with the Establishment of a Symptom Complex, Brain **33**:236, 1910.

2. Berger-Erdheim: Hypophysengeschwülste u. Hirncholesteatomen, Sitzungsb. d. k. Akad. d. Wissensch. **113**:537, 1904.

3. Bregmann-Steinhaus: Zur Kenntniss d. Geschwülste der Hypophyse u. Hyphophysegegend, Virchows Arch. f. path. Anat. **188**:210, 1907.

4. Russell, J. S., cited by Orzechowski and Mitkus: Rev. neurol. **2**:1, 1925.

5. Claude and Schaeffer: Tumeurs du troisième ventricule avec compr. hypophys. et sans syndrome infundibulaire, Rev. neurol. **37**:25, 1921.

6. Thomas; Jumentié, and Chausseblanche: Léthargie intermittente traduisant l'existence d'une tumeur du troisième ventricule: étude anatomoclinique, Rev. neurol. **30**:512, 1923.

7. Sainton and Peron: Épithélioma du lobe antérieur de l'hypophyse à symptomatologie cérébrale sans reaction hypophysaire, Rev. neurol. **30**:277, 1923.

8. Cuel, J.: Tumeur de l'hypophyse à symptomatologie mentale, Rev. neurol. **1**:564, 1924.

In 1924, Nyssen and I [9] reported the first observation of a tumor in the pituitary region in which the evolution of an adiposogenital syndrome was intimately associated with that of a parkinsonian and thalamic syndrome. This association appeared to us to be characteristic, and "if the location in the infundibulotuberian region, in the neighborhood of the nucleus thalamicus internus, the pyramidal tract and the pes pedunculi cerebelli superior, is sufficient to explain the phenomenology, the association of this late parkinsonian syndrome with an infundibulothalamic one appears to confer a definite clinical individuality on the morbid appearance."

In the discussion that followed this presentation, Orzechowski [10] reported a similar syndrome caused by a malignant growth in the pituitary gland, which infiltrated through the floor of the third ventricle and developed in the ventricular cavity.

In 1925, Orzechowski and Mitkus [11] reported a new case and described this clinical entity in detail, with a review of the literature. They pointed out that some pituitary tumors grow deeply, filling the third ventricle and usually determining marked dilatation of the whole ventricular system. These are tumors developing from the pouch of Rathke; they are frequently cystic and contain calcareous deposits. Because of the preponderance of the intraventricular portion, these tumors are often classified as tumor of the third ventricle or infundibular tumors. A complete study of my first case and an analysis of a new case permit a description of the evolution of this special clinical variety.

REPORT OF CASES

CASE 1.—*History.*—The personal history was unimportant. The right eye had been enucleated because of a chronic iridocyclitis seventeen years before the patient consulted me. The present illness began in 1921 with epileptiform seizures accompanied by marked vasodilatation in the face, which after severe attacks would persist for ten or twelve hours. All the fits started in the left limbs and spread rapidly to the face. They frequently varied greatly, sometimes as many as ten, twelve or fourteen fits occurring in a day.

Impotence was first noticed about the end of 1921 and became complete by January, 1922. In November, 1921, the patient weighed 64 Kg.; in March, 1923, the weight was 91 Kg. In April, 1923, the patient consulted Dr. Brandes because of failing vision; examination then revealed early optic atrophy, without papilledema, and bitemporal hemianopia. At the same time, he complained of occipital headache.

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9. Van Bogaert, Ludo; and Nyssen, R.: Tumeur de la région hypophysaire avec syndrome parkinsonien, Comptes rend. Congrès alién. et neurol. langue Franc., 1924, p. 263.

10. Orzechowski, in discussion on Van Bogaert and Nyssen (footnote 9, p. 268).

11. Orzechowski, C., and Mitkus, W.: De la forme parkinsonienne des tumeurs de la région infundibulo-hypophysaire, Rev. neurol. **2**:1, 1925.

The patient came under my observation in December, 1923. Adiposity was present, though it was less marked than before. Impotence was absolute.

Examination.—Temporal hemianopia was still present, though vision was almost lost. Choked disks and loss of pupillary reflexes were present; movements of the eyes were normal though both vertical and horizontal nystagmus was noticed.

Extrapyramidal System: A parkinsonian attitude was obvious; the head was slightly flexed and the face expressionless; the elbows were adducted, the wrists semiflexed, the fingers extended on the metacarpals and the thumb extended and adducted; there was a slight, discontinuous tremor of the thumb and fingers of the parkinsonian type; the lower extremities were extended and the feet externally rotated; the muscles in the arms showed a distinct jerking in relaxation; the patient did not make spontaneous movements and was unable to raise himself, though paralysis was not present; when raised passively, he fell without control

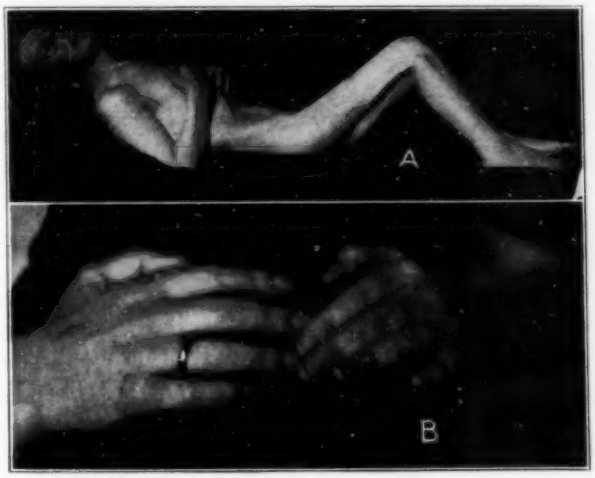

Fig. 1.—*A*, appearance of patient, showing the flexion paraplegia. *B*, appearance of hand, showing the spindle-shaped and slightly edematous fingers.

if the support was released; all movements, however, were possible and segmentary power was not diminished.

Pyramidal System: The tendon reflexes in the legs were exaggerated, with foot clonus on both sides; the masseter reflex was brisk; the right plantar reflex was of the extensor type; the cremasterian reflexes were present, but the abdominal reflexes were diminished. Tremor without a disturbance of movement was present in the tongue. Cerebellar signs were not present.

For several weeks before admission, the patient had experienced severe pain in the left side of the face and at the root of the right leg. During his stay in the hospital, he experienced crises of burning and crushing pain in the right leg and groin, which he compared with the pain previously experienced in the left side of the face. Marked hyperalgesia of the skin was present over the area in which the pains occurred, and even the friction of the blankets was extremely painful.

Course.—After December, 1923, the condition became progressively worse. Cachexia of "meager" type developed; rigidity was more marked, the legs becoming flexed and the arms adducted to the body; passive extension was still

possible in the left leg, but the right became ankylosed in flexion by tendinous retraction (fig. 1 *A*). Tremor persisted; it occurred sometimes when the patient was at rest, but became marked during motion and was thus more intentional and global. The head became hyperextended and was turned sometimes to the right and sometimes to the left; in either position it was rigid and movable only with difficulty. Spasmodic crying occurred rarely. The evidences of involvement of the pyramidal tract persisted; rectal and vesical incontinence were complete. Swallowing became difficult, and the patient rarely spoke.

Distinct trophic disturbances also appeared; the skin of the lower parts of the leg became ichthyotic and desquamated in small scales; the legs were always cold, and symmetrical, livid areas appeared on the knees; the fingers were spindle-shaped and slightly edematous, and the skin was smooth and supple; the nails appeared normal (fig. 1 *B*).

Lumbar puncture produced a clear fluid, with a pressure of 32 cm. by the Claude apparatus; its cytologic and chemical characters were normal. The Guillain reaction was negative, and the Bordet-Wassermann reaction was negative with both the blood and the spinal fluid.

General physical examination revealed nothing abnormal, though the testes were distinctly small. Polyuria or glycosuria were not present; the urinary output was from 1,200 to 1,440 cc. in twenty-four hours.

Sugar Metabolism: The glucose threshold, estimated by a glucose meal on three occasions, was raised. Three hundred grams of glucose was administered and was followed by an injection of one half of a posterior lobe. Sugar did not appear in the urine during the next twenty-four hours, though examinations were made every half hour for the first four hours.

The basal metabolic rate was — 18 per cent. The thermoreaction of Franckl-Hochwart was negative with two tests. The oculocardiac reflex showed a slowing of 12, 11 and 14 beats in successive tests. Injections of pituitary extracts did not produce changes.

The neurologic condition continued much the same. The mask-like condition of the face was fixed; tonic neck reflexes were not observed. Death occurred in October, 1924.

Necropsy.—Numerous calcified peribronchial glands were present, with pleurisy at the right base and adhesions over the right apex. The liver was small and sclerotic. The thyroid and suprarenal glands were of normal size. The testes were small and fibrous; the epididymis was retracted; the prostate was small and sclerotic.

On the ventral surface of the brain there was a hard, nodular tumor the size of a pigeon's egg, embracing the chiasma and flattening out the optic nerves which were pushed laterally and backward (fig. 2). At the posterior part of this mass was a white stem, which on section contained a cavity filled with small friable granulations; this stem was the pituitary root. A slightly paramedian sagittal section showed a cauliflower-like tumor, with colloid cavities filled with a greenish fluid; the tumor issued from the infundibulum and filled the cavity of the third ventricle, compressing the gray nuclei on both sides, and passed forward to invade the lateral ventricles which were also greatly dilated (fig. 3). Posteriorly, the tumor terminated at the level of a section through the most anterior part of the red nuclei. The pituitary gland was macroscopically intact.

Histologic Study.—The Tumor: The structure was complex and presented: (*a*) pseudo-adamantine papillae with a lining of elongated cells at the periphery of the papillae near which were bands of connective tissue which in places had undergone myxoid transformation (fig. 4 *A*); (*b*) cystic areas delimited by

Fig. 2.—Ventral face of the brain, showing the tumors embracing the chiasma.

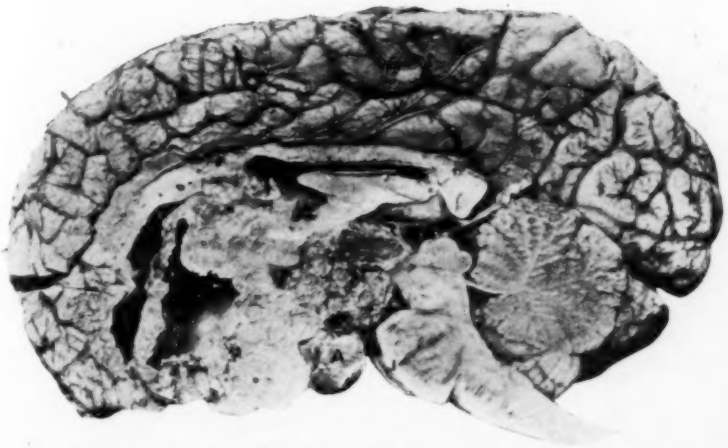

Fig. 3.—Sagittal section of the brain, showing the tumor filling the third ventricle and dilating the anterolateral ventricles. The pituitary gland (*A*) seems to be intact.

slender epithelial trabeculae, the cavities being lined with cylindric epithelium and filled with colloid material (fig. 5); (*c*) areas of calcified malpighian epithelium which stained deeply and which were arranged in onion-like layers with a calcified center and hyaline and granular degeneration (fig. 4 *B*) in the layer cells; in other places, the hyperchromic bodies appeared to have arisen from connective

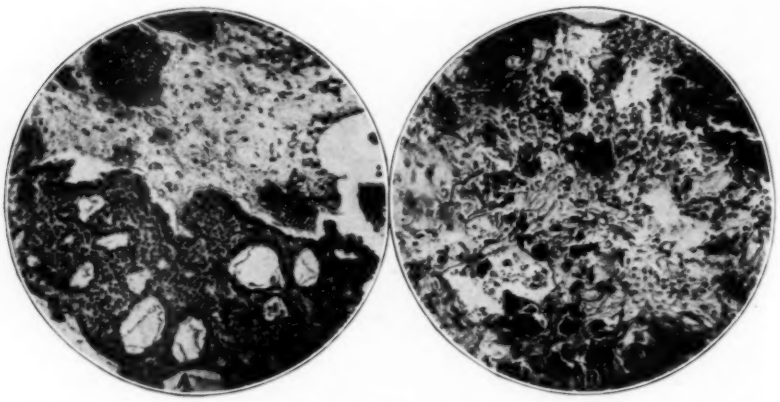

Fig. 4.—*A*, pseudo-adamantine papillae and myxoid transformation of connective tissue. *B*, areas with calcified malpighian epithelium.

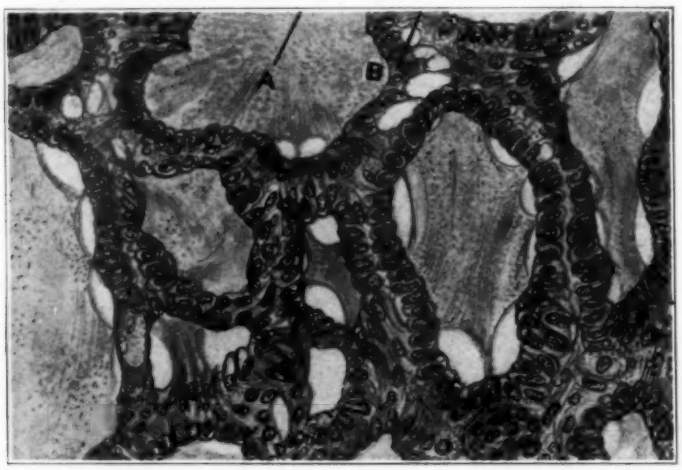

Fig. 5.—Cystic areas limited by cylindric epithelium (*B*) and filled with colloid material (*A*).

tissue by agglutination and keratinization of collagen fibrils (fig. 6). The tumor had developed from the embryonic rests of the pituitary canal, but was of mixed type; it included the structure of a cyst of Rathke's pouch with that of a pharyngopituitary epithelioma.

Endocrine Glands: The thyroid vesicles were filled with colloid containing many vacuoles, and the interlobar connective tissue was scanty. The parathyroid glands did not contain oxyphil cells and only a scanty deposit of fat; numerous

colloid vesicles were present. No vestige of thymus was found. The suprarenal capsule was slightly thickened, and the cortical trabeculae were more fibrous than normal; the glomerular zone showed markedly granular and eosinophilic cells, but few vacuoles were present; the fascicular and reticular areas were normal. The testes showed diminution of interstitial cells and absence of spermatogenesis; the epithelial lining of the seminal tubules was pluristratified in places. The pancreas and prostate were normal. The liver showed early annular sclerosis, which was especially periportal in distribution.

Fig. 6.—Between the colloid (*A*) and cystic areas (*B*), the connective tissue appears keratinized (*C*).

Pituitary Gland: The anterior lobe was well preserved with a predominance of oxyphil cells, few undifferentiated cells and no mast cells; the colloid cavities were preserved (fig. 7 *A*). The most median section passed through the insertion of the infundibular stem; a highly vascular glioconnective tissue extended through the posterior two thirds of the glandular lobe in its highest part and spread through the anterior part of the lobe; this was an exaggeration of the normal (fig. 7 *B*). The pars intermedia showed well developed colloid cavities; the basic and neutrophil cells from which they arose had invaded the neural lobe in places. The neural lobe appeared normal except that the perivascular tissue seemed more abundant than usual; hyaline bodies were not present. The infundibulum was normal; the surrounding fibrous layer, which was continuous with the capsule of the gland, was thicker than normal.

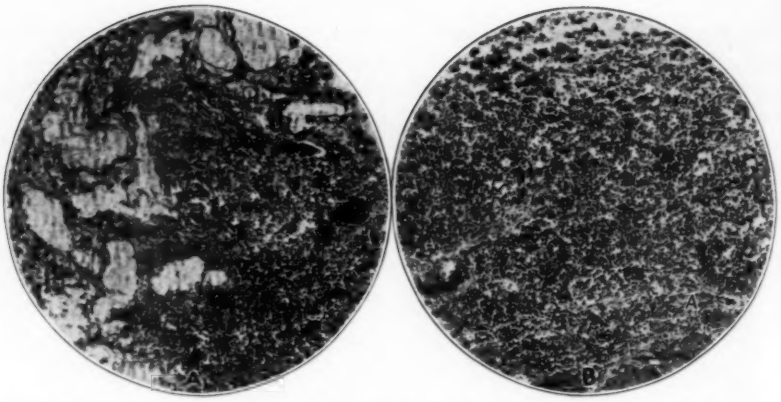

Fig. 7.—*A*, pars intermedia of the pituitary gland; preservation of the colloid cavities; *B*, glandular lobe (most median section); exaggeration of the normal glioconnective tissue in the highest part of this lobe (*C*).

Fig. 8.—Transverse section of the brain through the tuberian region: *A* shows the tumor filling the third ventricle; *B*, depression of the internal thalamic nucleus; *C*, destruction of the nuclei of the optic chiasma and the ventral nucleus of the tuber.

Nervous System: The medulla was normal. The bulb showed marked infiltration with amyloid bodies around the lower cranial nerves, with peri-ependymal and subependymal reactions, especially on the anterior surface and in the superior third. The bulbar nuclei were normal.

The pons, cerebellum, peduncles, red nuclei and locus niger did not show lesions, except meningeal infiltration.

The ventricles were greatly distended. The caudate nucleus, the central gray matter, the internal capsule and the lenticular nucleus were pushed aside. The anterior perforated space and the orbital portion of the second and third frontal convolutions were reduced to a thin whitish thread over the neoplastic nodules. The third ventricle was filled and distended laterally by the tumor mass. The atrophied chiasma was embedded in the tumor.

A section through the tuberian region (fig. 8) illustrates this condition. Attention may be called to the depression of the internal thalamic nucleus.

Histologic study of the gray matter around the third ventricle revealed marked rarefaction of cells in the internal nucleus of the thalamus (fig. 9 *A*) and hyperchromia in the internal nucleus and the inferolateral part of the external nucleus (fig. 9 *B*). In the globus pallidus, hyperchromic atrophy of the cells with multiplication of neuroglia nuclei throughout the internal segment was present.

Careful study failed to reveal any trace of the nuclei of the optic chiasm or of the ventral nucleus of the tuber except in the paramammillary portion. Lesions were well marked in the juxtatrigonal periventricular nucleus (fig. 10).

Though the frontal cortex was greatly reduced in thickness, the cyto-architectonic disturbances were slight. There was no apparent degeneration in the frontopontile bundle.

Summary.—A suprapituitary tumor gave rise, first, to an adiposogenital syndrome with disturbance of glycoregulation; this was soon complicated by a thalamic syndrome and later by a parkinsonian syndrome. Anatomic study revealed a large tumor of the adamantinoma type which had apparently developed at the expense of the original superior epithelial cells of the infundibulum; from there it had invaded the tuberian floor, filled the cavity of the third ventricle and pushed the thalamic masses aside laterally; it had invaded the lateral ventricles, which it distended greatly, and had pushed aside the white substance of the frontal pole and the central gray nuclei. Histologically, the pallidum showed marked lesions; the pituitary gland was intact.

Case 2.—*History.*—Mrs. F., aged 46, the mother of three healthy children, for four years had suffered intense pain in the upper limbs, with vague, ill localized headache. Vision had been practically lost on several occasions. For four months she had had epileptic crises at irregular intervals with an aura consisting of marked vasodilatation of the whole head. Pain in the hands became continuous and intolerable, and the patient was confined to bed. Slight deformity appeared in the hands: they were wasted, and extension of the fingers became impossible. For a year, vision had been failing and the patient complained of pain in the left orbit. Vomiting had occurred a few times with headache. Urination was frequent and abundant.

Physical Examination.—Slowness of movement and a slight tremor of the fingers were striking. The hands were deformed and suggested both chronic

rheumatism and parkinsonism. The patient moved "all in one piece;" if placed erect, she fell backward without the slightest defensive movement. Mimicry was much diminished.

Disturbance of the pyramidal function was not found, but the reflexes of defense were greatly exaggerated. Objective sensory disturbances were not found; diffuse hyperesthesia of both forearms and of the thorax, especially to

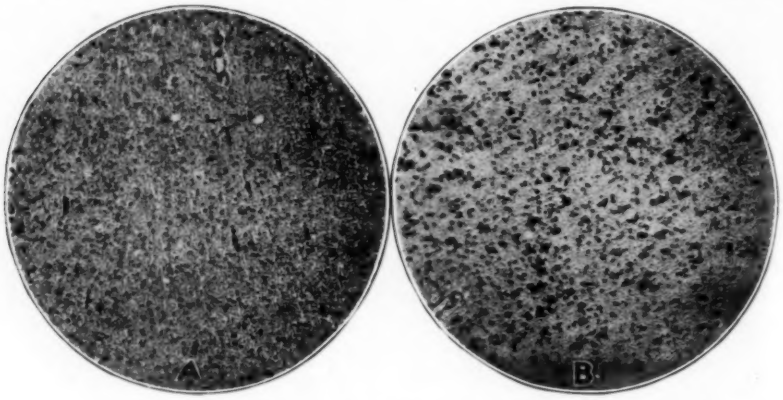

Fig. 9.—*A*, marked cellular rarefaction in the internal thalamic nucleus. *B*, hyperchromia and cellular disintegration in the internal nucleus and inferolateral part of the external thalamic nucleus.

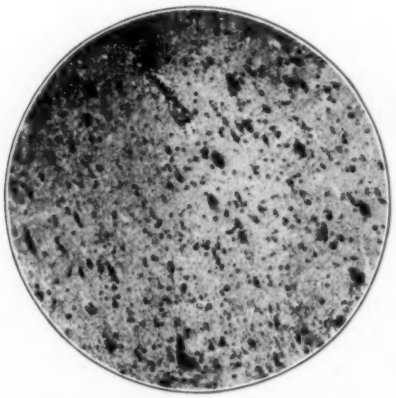

Fig. 10.—Important cellular lesion in the juxtatrigonal periventricular nucleus of the tuber.

cold stimuli, was accompanied by tearing, crushing pains that were extremely resistant to analgesics, even in large doses. The vasomotor reflexes were preserved in the hyperesthetic areas.

Marked hypersomnia was present, the crises of lethargy being accompanied by amnesia which was sometimes retrograde.

The amount of urine varied from 6 to 7.2 liters daily. Glycosuria was not present, but the glycemic curves showed delay in appearance and a low rise.

The cranial nerves did not show any abnormality. The optic disks showed choking, and vision was reduced to one-half on both sides. Roentgenograms showed no enlargement of the sella turcica, erosion of the posterior clinoid processes and a shadow beneath the pituitary gland.

The Bordet-Wassermann reaction with the blood was negative. Lumbar puncture yielded a slightly yellowish fluid with an initial pressure of 90 cm. (Claude) and a terminal pressure, after removal of 12 cc., of 43 cm.; the cell count was 2 per cubic millimeter, and the albumin, 0.70; the Bordet-Wassermann reaction was negative. The basal metabolic rate was —26 per cent.

Summary.—During four years, the development of a syndrome of intracranial hypertension led rapidly to a thalamo-infundibular syndrome. The infundibular symptoms were polyuria, disorder of glycoregulation and crises of narcolepsy with onirism, fabulation and retrograde amnesia. The thalamic symptoms were pains, hyperesthesia to cold and trophic changes in the extremities. The extrapyramidal syndrome was represented by slowness, retropulsion and tremor. Roentgen-ray examination confirmed the existence of a tumor above the pituitary gland.

COMMENT

The two cases reported belong in the same group—both showed an infundibulothalamic and later an extrapyramidal phase. The evolution and grouping of the symptoms establish a particular clinical type of infundibular tumor.

The Thalamic Syndrome.—The thalamic symptoms are prominent, early and of rapid evolution; the patients complain of severe pain of the central type, with trophic disturbances which are still in need of further study and with the hyperalgesia to cold that has been described by Pierre Marie and Bouttier.[12] The anatomic changes in the thalamic nuclei in case 1 are in accord with the view that the internal nucleus is concerned with the etiology of thalamic pains. Similar clinical disturbances in the case of Orzechowski and in case 2 of Weissenburg correspond with the same lesion. In my opinion, absence of evident lesions in the thalamus in cases of thalamic syndrome must be due to failure to make a systematic and detailed histologic study.

The Parkinsonian Syndrome.—In case 1, which were the anatomic lesions responsible for the parkinsonian syndrome?

The white substance was marked by compression through intraventricular prolongations of the tumor; on the other hand, the central gray nuclei were compressed by the tumor at the level of the third ventricle. The presence of this double lesion again raises the question of the anatomophysiologic problem of parkinsonism, concerning which

12. Marie, Pierre, and Bouttier: Études sur les troubles sentitifs, Rev. neurol. **29**:115, 1922.

there are two favored views: frontal and optostriate. A preliminary clinical distinction is necessary. In the study of infundibular tumors as well as frontal tumors, one must reserve the title of parkinsonism (and consequently the discussion of its pathogenesis) to cases in which the syndrome is complete: typical tremor, salivation, typical attitude of the body, amimia, propulsion or retropulsion and rigidity. The title should not be used to characterize a fragmentary extrapyramidal syndrome such as that in case 2, in which amimia, retropulsion and an effective tremor may be the only semeiologic signs of extrapyramidal disturbance. It is well known that lesions of the frontal pole suffice to explain such features; everyone has observed similar apathy, akinesia, amimia and disorder of equilibrium in frontal tumors; these symptoms suggest but do not rigorously belong to parkinsonism. With this understanding the question remains, whether a tumor of the frontal pole may by itself provoke a true parkinsonism.

Several cases have been reported in the literature. In that of Rebattu and Ferrier,[13] histologic details were not given; in that of Bostroem,[14] a report was not made of the microscopic study of the red nucleus; in that of Schuster,[15] the frontal endothelioma was accompanied by histologic modifications in the gray nuclei. The most recent observation, that of Dimitz and Schilder,[16] did not include an anatomic study. None of the cases in the literature, therefore, permits the correlation of a complete parkinsonian syndrome with a pure frontal lesion. Of course, I do not deny the part played by the prefrontal cortex in certain disturbances of voluntary contraction such as their myotonic persistence demonstrated by Kleist [17] in certain akinesias outlined by Foerster.

In case 1, histologic examination demonstrated important pallidal lesions with integrity of the "nigerian" and "dentate" systems. From the standpoint of pathogenesis, our case must be considered in relation with those of Stertz [18] (parkinsonian syndrome from a tumor of the base pressing against the basal nuclei), Parker [19] (infiltrating glioma of

13. Rebattu and Ferrier: Tumeur du lobe frontal ayant realisé cliniquement le tableau habituel de l'encéphalite épidémique, Lyon méd. **130**:347, 1921.

14. Bostroem: Zur Diagnose der Stirnhirntumoren, Deutsche Ztschr. f. Nervenh. **70**:82, 1921.

15. Schuster, Paul: Kann ein Stirnhirntumor das Bild der Paralyse agitans hervorrufen? Ztschr. f. d. ges. Neurol. u. Psychiat. **77**:1, 1922.

16. Dimitz and Schilder: Zur Symptomatologie der Stirnhirntumoren, Med. Klin. **9**:36, 1922.

17. Kleist, T.: Zur Auffassung der subcorticalen Bewegungstörungen, Arch. f. Psychiat. **59**:310, 1921.

18. Stertz: Die Encephalitis epidemica, Berlin, Julius Springer, 1922, p. 210.

19. Parker: Tumors of the Brain Simulating Epidemic Encephalitis and Involving the Third Ventricle, the Fourth Ventricle and Basal Ganglia, J. Nerv. & Ment. Dis. **58**:32, 1923.

the central ganglia and subthalamic floor with parkinsonian syndrome), Claude and Schaeffer [5] and Alajouanine (gliomas of the central ganglia on the right).

A last question concerning certain recent theories of parkinsonism is: Can a frontal lesion itself cause the anatomic disorders observed in the optostriate nuclei or does the frontal pole exert a dynamic influence on the central ganglia through the frontopontile bundle of Kleist?

Because of the size of the lesion and the extent of its area of compression, our case does not permit a conclusion on this point any more than do those of Schuster; to form a conclusion, one must limit the study to focal lesions of slight extent in the anterior pole, and this work yet remains to be done. It should be remembered, however, that the true parkinsonian syndrome observed in our case must be related to a pallidal lesion, according to the views of F. H. Lewy,[20] C. and O. Vogt,[21] Foix and Nicolesco [22] and Schuster.[15]

The Glycoregulatory Disturbances.—One of the principal elements of the infundibulotuberian syndrome is disorder in carbohydrate metabolism. Glycosuria was not observed in my patients. Nevertheless, determinations by the Fontès-Thivelle method yielded glycemic values of 0.151, 0.160, 0.165, 0.130 and 0.185, with an average of 0.161. By the same method, the average values of the control subjects is from 0.105 to 0.118. Consequently, a somewhat marked hyperglycemia was present in our two cases. Sachs and MacDonald [23] have shown that the glycemic value increases slightly after operations on the pituitary or infundibular region, and Gournay and Legrand [24] have established the hypothesis that glycemia is definitely elevated after lesions of the paraventricular nuclei even before the onset of glycosuria. In our second patient, marked polyuria without glycosuria was present, and was uninfluenced by administration of posterior pituitary extract.

A sugar tolerance test performed on three occasions gave the curves illustrated in figure 11, the dotted line being that of a control subject. It will be noted that the curve is distinctly higher and is certainly delayed;

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20. Lewy, H.: Zur pathol. Anat. der Paralysis agitans, Ztschr. f. Nervenh., 1914, vol. 50.

21. Vogt, C., and Vogt, O.: Zur Lehre der Erkrankungen des striären Systems, J. f. Psychol. u. Neurol., 1920, vol. 25.

22. Foix and Nicolesco: Les noyaux gris centraux, Paris, Masson et Cie, 1926, p. 493.

23. Sachs, Ernest, and MacDonald, M. E.: Blood Sugar Studies in Experimental Pituitary and Hypothalamic Lesions, Arch. Neurol. & Psychiat. **13**:325 (March) 1925.

24. Gournay and Legrand: Études expérimentales sur le diabète insipide infundibulaire et le diabète sucré tubérien, Ann. méd. **18**:434 (Dec.) 1925.

it recalls the cures reported by Marcel Labbé [25] in certain diabetic patients. These results are identical with those of Gray,[26] Hamman and Hirschmann [27] and Cushing,[28] and with the experimental results of Houssay, Hug and Malamud [29] and Sachs and MacDonald.[23] Major [30] and Wilder, Russell and Sansum,[31] however, failed to observe this delay and elevation of tolerance. Delayed increase of glycemia has been noted recently by Critchley and Ironside, but the delay was less marked than usual.

The alimentary hyperglycemia was not accompanied by glycosuria in my cases. The elevation of the threshold of sugar tolerance is demonstrated by the glycosuria test described by Parisot and Richard, in which

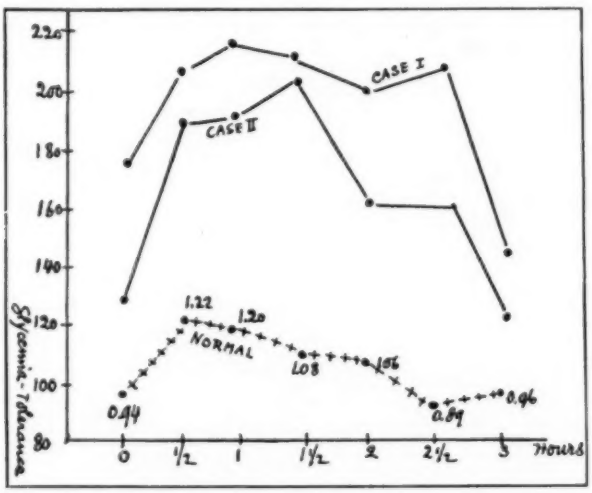

Fig. 11.—Curves of sugar tolerance in the two cases of suprasellar tumor and in a normal subject.

25. Labbé, Marcel: Le diagnose de l'hyperthyroidie, épreuve de l'hyperglycemie alimentaire et du métabolisme basal, Rev. franç. d'endocrinol. **97**:108 (May) 1923.

26. Gray, Horace: Blood Sugar Standards, Arch. Int. Med. **31**:245 (Feb.) 1923; cited by Sachs and MacDonald (footnote 23).

27. Hamman and Hirschman: Studies on Blood Sugar, Arch. Int. Med. **20**: 761 (Nov.) 1917; cited by Sachs and MacDonald (footnote 23).

28. Cushing, Harvey: Carbohydrate Tolerance and the Posterior Lobe of the Hypophysis Cerebri, Bull. Johns Hopkins Hosp. **22**:165, 1911; cited by Sachs and MacDonald (footnote 23).

29. Houssay; Hug, and Malamud: Pituitary Body and Carbohydrate Metabolism, Rev. A. soc. méd. Argent. **34**:1128, 1921; cited by Sachs and MacDonald (footnote 23).

30. Major: Studies on Sugar Tolerance, Bull. Johns Hopkins Hosp. **34**:21, 1923; cited by Sachs and MacDonald (footnote 23).

31. Wilder, Russell and Sansum: Glucose Tolerance in Health and Disease, Arch. Int. Med. **19**:311 (Feb.) 1917; cited by Sachs and MacDonald (footnote 23).

pituitary was given to provoke the glycosuria. Following their technic in our cases, I did not observe a trace of sugar in the urine.

In case 1, it was impossible to determine the rôle played by the cirrhosis of the liver in the disturbances of carbohydrate metabolism; in the second patient, however, there was no suggestion of any disease of the liver. It seems permissible, therefore, to ask whether the disorder in glycoregulation did not have its origin in the tuberian dysfunction. Recently, Nicolesco and Raileanu [32] have demonstrated important cellular lesions in the tuberian ventricular nuclei in a case of diabetes.

It seems evident that an intimate physiopathologic relation, the exact nature of which is still undetermined, exists between infundibulotuberian lesions and glycoregulatory disturbance.

The Endocrine Disturbances.—The first of the patients reported at first presented an adiposogenital dystrophy with a mild dystrophy of peculiar type at the end of the course. Experimental study of the hypothalamic nuclei has demonstrated that they have a rôle in the development of the gonads; [32] in addition, it seems that the hypothalamus regulates fat metabolism to some extent; Jean Camus believes this to be dependent on the function of the paraventricular nucleus.[33]

Precise data on the topography of these centers are lacking, but experimental study has shown that in different cases, most probably depending on the exact localization of the nerve lesion, adiposity with genital atrophy and abolition of sexual appetite may develop; genital atrophy without adiposity and adiposity without genital atrophy may occur; I would add to these symptoms a special "pituitary cachexia" or, rather, "infundibular cachexia," which Bailey and Bremer [34] were the first to demonstrate.

The infundibular tumors with verified integrity of the pituitary gland that have been reported so far may be classified into: those associated with adiposogenital syndrome and loss of sexual appetite—the cases of Erdheim,[35] Bartels,[35] Vigoroux and Delmas,[36] Falta and Nonne, Nonne and Hirsch, Strenberg,[37] Armstrong [38] (case 2), Lereboullet,

32. Nicolesco and Raileanu: A propos de lésions du système nerveux central dans le diabète sucré, Rev. neurol. **34**:31, 1927.

33. Binet, Leon: Recherches sur les centres du tuber cinereum et sur la glande hypophysaire, Ann. méd. **18**:407, 1925.

34. Bailey, P., and Bremer: Experimental Diabetes Insipidus, Arch. Int. Med. **28**:773 (Dec.) 1921.

35. Quoted in Agostini: Sui tumori della regione infondibulare, Manicomio provinciale di Perugia, 1924.

36. Vigouroux and Delmas: Nouv. iconog. de la Salpêtrière, 1901, vol. 3.

37. Quoted in Miller, V.: Dystrophia adiposogenitalis bei Hypophysenzysten, Virchows Arch. f. path. Anat. **36**:54, 1922.

38. Armstrong: Three Cases of Suprapituitary Tumor Presenting Fröhlich's Syndrome, Brain **45**:113, 1922.

Mouzon and Cathala,[39] Ricaldoni, Pfeiffer, Cassirer-Lewy,[35] and Thomas, Jumentié and Chausseblanche;[6] (2) those associated with pure adiposity—the cases of Bregmann-Steinhaus, Kankeleit,[40] Rodolphe Ley[41] and Parker.[19] Sometimes feminism is present, as in the case of Zack.[42] Sometimes the tumors are associated with genital atrophy but without adiposity, as in the case of Berger-Erdheim,[2] and (4) with "meager cachexia," though I do not know of any cases of this type.

In our first case, the adiposogenital dystrophy gave place to a peculiar trophic evolution. In large cerebral tumors, as a rule, marked loss of weight undoubtedly is present, especially when there is frequent vomiting. This was not true in the case reported. The loss of weight was associated with other trophic disturbances. In March, 1923, the weight was 91 Kg.; in January, 1924, it was 38 Kg. In addition to the loss of weight, generalized cutaneous ichthyosis, with exfoliation of the hands, extensive, symmetrical "livid spots" from the knees to the ankles, slight edema of the fingers which gave them a spindle shape and masked the loss of adipose tissue, and constant hypothermia were present. The condition remained the same for seven months, and death resulted from an intercurrent disease.

All these symptoms belong as much to the "meager cachexia" of Simmond as to the pituitary cachexia. Urechia and Mihalescu[43] and Urechia and Elekes[44] have recently brought clinical confirmation to the experimental results of Bailey and Bremer, showing that in cases of pituitary cachexia the nuclei of the tuber show marked alteration, while the other glands of internal secretion presented changes insufficient to account for the cachexia. They reported intense, but not exclusive, changes in the suprachiasmatic and paraventricular nuclei.

Studies of basal metabolism twice showed lowering of the rate. Such lowering in the course of an adiposogenital dystrophy is in accord with the observations of Means,[45] Boothby, Maranon and Carrasco,[46]

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39. Lereboullet, Mouzon and Cathala: Infantilisme dit hypophysaire par tumeur du troisième ventricule, intégrité de l'hypophyse, Rev. neurol. **37**:154, 1921.

40. Kankeleit: Zur Symptomatologie, pathologische Anatomie und Pathogenese von Tumoren der Hypophysengegend, Arch. f. Psychiat. **58**:789, 1917.

41. Ley, Rudolphe: Tumeur de l'infundibulum. Intégrité de l'hypophyse. Syndrome adipeux, Rev. neurol. **38**:1377 (April) 1922.

42. Zack: Ueber Hypophysistumoren, Wien. klin. Rundschau **8**:165, 1904.

43. Urechia and Mihalescu: La dystrophie maigre, Rev. neurol. **1**:73 (Jan.) 1926.

44. Urechia and Elekes: La cachexie dite hypophysaire, Encéphale **31**:353 (May) 1926.

45. Means: Studies on the Basal Metabolism in Obesity and Pituitary Disease, J. M. Research **32**:21, 1915.

46. Maranon and Carrasco: Sur la valeur clinique de la détermination du métabolisme basal, Ann. de méd. **13**:124, 1923.

Montes,[47] Labbé, Stevenin and van Bogaert.[48] In a case of acromegaly complicated by a tuberian syndrome, Cestan, Sendrail and Lasalle[49] observed lowering of the metabolic rate and questioned whether the tuberian changes were not the cause of this anomaly. The basal metabolic rate in our second patient was also low.

Whatever the origin of the adiposogenital syndrome (infundibular or pituitary) may be, adamantinomas above the pituitary gland are not accompanied by acromegaly or giantism, while acromegaly is evident in reports of six cases of intrasellar tumors collected by Critchley and Ironside. In all four of the cases reported by those authors, the patients were infantile and adipose.

CONCLUSIONS

1. Suprapituitary tumors may exhibit a thalamic and parkinsonian appearance following the stage of their intraventricular growth. The predominance of one or the other of these symptoms is sufficiently evident in some cases to justify the terms "thalamic" or "parkinsonian" forms.

2. The thalamic syndrome must be referred to destruction of the internal nucleus of the thalamus; the true parkinsonian syndrome, to a lesion of the pallidum. Some extrapyramidal disturbance must be attributed to functional troubles in the frontal pole as the result of dilatation of the lateral ventricles from neoplastic extension.

3. During the infundibular phase glycoregulation is, as a rule, disturbed and may be diminished. The meaning of this is not established. In my first case, a definite lesion of the periventricular nucleus in the tuber was present.

4. The endocrine disturbances are almost always characterized by an adiposogenital dystrophy which may later evolve into a marked "meager cachexia."

5. The histopathologic integrity of the pituitary gland in my first case is of great biologic interest in relation to the disturbance of glycoregulation, the disorder of fat metabolism and the regulation of sexual function.

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47. Montes, Pareja: Pituitary and Basal Metabolism, Ann. Fac. Med. Montevideo **8**:1102 (Dec.) 1923; **13**:364 (March) 1925; quoted by Sachs and MacDonald (footnote 23).

48. Labbé, Marcel; Stevenin, and van Bogaert: Le métabolisme basal dans les syndromes hypophysaires, Ann. de méd. **3**:258, 1925.

49. Cestan, Sendrail and Lasalle: Contributions a l'étude du métabolisme basal chez les acromégales, Rev. neurol. **1**:1 (Jan.) 1926.

PINEAL PATHOLOGY

FURTHER STUDIES *

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AND
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BOSTON

The function of the pineal body in the human organism is still a subject of controversy. By some it is considered to be a gland of internal secretion; by others, a vestige of the median eye of certain reptilian forms. No one believes now in the suggestion of Descartes that it might be the seat of the soul, but numerous phylogenetic, embryologic, histologic and clinicopathologic studies, as well as experiments in feeding and extirpation, have not succeeded in establishing definitely its function.

Tilney and Warren [1] believe that they have demonstrated a glandular structure in the pineal body of the human embryo, and von Volkmann [2] thinks that he has found secretory granules in the pineal cells. On the other hand, Hortega [3] cannot find evidence of secretory activity in either the neuroglia or pineal parenchyma, and he believes that the granules found by von Volkmann are blepharoplasten akin to those of the ependymal cells. The older notion, based on histologic studies, that the pineal body undergoes an involutional change at puberty seems to be definitely abandoned (Uemura [4] Berblinger [5]).

Results of feeding and extirpation experiments on animals are contradictory and inconclusive, as are also the clinicopathologic observations. They have recently been the subject of an exhaustive review by Berblinger,[5] who is obviously correct when he insists that in the search for the function of the pineal body physicians are still at the stage of collecting evidence, and it is for this reason that the following three clinical records and pathologic reports are published.

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* From the Surgical Clinic and Laboratory of Dr. Harvey Cushing, Peter Bent Brigham Hospital.

* Read at the Fifty-Third Annual Meeting of the American Neurological Association, Atlantic City, N. J., May, 1927.

1. Tilney and Warren: The Morphology and Evolutionary Significance of the Pineal Body, Am. Anat. Mem., Philadelphia **9**:7, 1919.

2. Von Volkmann: Histologische Untersuchungen zur Frage der Sekretionsfunktion der Zirbeldrüse, Ztschr. f. d. ges. Neurol. u. Psychiat. **84**:593, 1923.

3. Hortega: Constitucion histologica de la glandula pineal, Arch. de neurobiol. **3**:359, 1922.

4. Uemura: Zur normalen und pathologischen Anatomie der Glandula pinealis usw., Frank. Ztschr. f. Path. **20**:381, 1917.

5. Berblinger: Die Glandula pinealis (Corpus pineale). Handbuch der speziellen pathologischen Anatomie und Histologie, Henke und Lubarsch, vol. 8, pp. 681-759.

The chief theory of pineal function assumes that a secretion from this organ inhibits puberty, and that an involutional change during puberty diminishes its secretion, thus allowing sexual characteristics and activity to appear. This theory derives some support from published reports of cases in which precocious puberty accompanied the destruction by a tumor of the pineal body in children (Horrax and Bailey,[6] and Bailey and Jelliffe[7]). The first case we have to report is an observation of this kind.

It might be pointed out that the patient was a boy; in fact, a case of pubertas praecox occurring in a girl has never been proved by necropsy to have been due to a tumor of the pineal body.

REPORT OF CASES

CASE 1.—*Pinealoma containing cartilage cells (teratoma?) associated with slight pubertas praecox. Development of testes corresponding to those in a person six years older than the patient.*

History.—On Aug. 20, 1925, L. T., a boy, 9 years of age, was referred to the Peter Bent Brigham Hospital by Dr. J. J. O'Brien of Schenectady, N. Y., with the complaint of headache and vomiting. The family and past histories were irrelevant. The boy had been well until July 4, 1925, when he had a mild headache, vomited and complained of double vision. Three days later, he vomited again and had a severe headache which lasted ten hours. Headache had been practically constant since that date and was frontal in location. Diplopia likewise persisted, and vomiting occurred once or twice a week. Three weeks before admission the gait became unsteady, and within one week was so poor that the patient had to take to bed. For the week previous to admission there was drooping of both upper eyelids.

Examination.—The boy's height was 128 cm., which is slightly greater than the average normal for this age. His testes were approximately 2 cm. in length, and the penis measured 5 cm. Percussion of the skull gave the typical cracked pot resonance of separated sutures. The pupils were small and equal, and they did not react to light or in accommodation. Vision was greatly reduced, the loss being out of all proportion to the appearance of the fundi, which showed early choking of 3 diopters on both sides without atrophy. Conjugate movements of the eyeballs upward were impossible above the horizontal plane. Both abducentes were weak, convergence was slight, and there was bilateral ptosis. There was a slight left lower facial palsy; hypotonia of both arms and both legs was marked, and the deep reflexes generally were diminished.

A diagnosis of probable pineal tumor was made, but it was thought advisable to perform a ventriculogram to confirm or refute this impression. On September 2, air was introduced into the lateral ventricles which were found to be dilated. In addition, these studies showed a rounded shadow, apparently a tumor, bulging forward into the third ventricle.

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6. Horrax, and Bailey, Percival: Tumors of the Pineal Body, Arch. Neurol. & Psychiat. **13**:423 (April) 1925.

7. Bailey, Pearce, and Jelliffe: Tumors of the Pineal Body, Arch. Int. Med. **8**:851 (Dec.) 1911.

Operation.—On September 9, Dr. Cushing exposed the region of the third ventricle by splitting the posterior end of the corpus callosum after the right cerebral hemisphere had been retracted laterally. A definite tumor was not disclosed. The patient survived this procedure a few days only, and a complete necropsy was permitted.

Necropsy.—A complete examination of the body was made seven hours post mortem. General examination disclosed infarction and necrosis of the lungs from pulmonary emboli, bilateral hemothorax and patent foramen ovale. The testes contained numerous spermatocytes but no spermatozoa, and rarely spermatids, although numerous mitoses could be seen in the spermatocytes. The interstitial cells were well developed in small clumps. The structure corresponded to that of a boy aged 14 or 15 years in active puberty (fig. 1). The testes

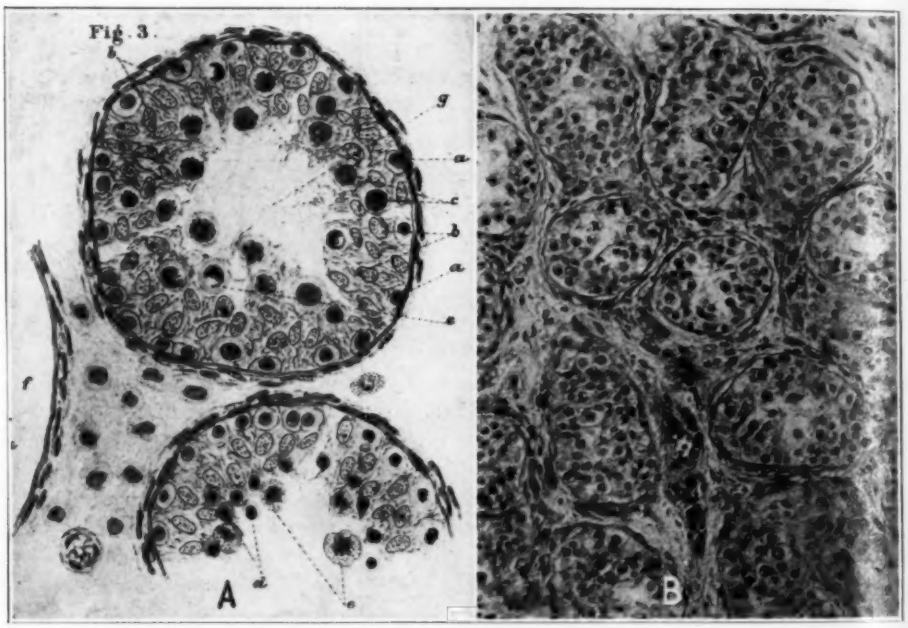

Fig. 1.—*A* shows testis of boy, aged 14; after Spangaro. *B* shows testis from patient in case 1, showing structure corresponding to that of a boy aged 14.

together weighed 12.5 Gm. The glands of internal secretion (hypophysis, thyroid, pancreas, suprarenals, parathyroid and thymus) were macroscopically and microscopically normal.

The cerebral ventricles were injected with a 10 per cent solution of the commercial solution of formaldehyde two hours before removal of the brain which was afterward immersed in the same solution of formaldehyde for further fixation. Externally were seen flattening of the convolutions, dilatation of the third ventricle and a nodule of what appeared to be a reddish tumor projecting downward from the fourth ventricle between the cerebellum and bulb. A median sagittal section of the brain was made passing through a large tumor extending from the splenium of the corpus callosum to the calomus scriptorius, probably arising from the pineal body, no trace of which could be seen. The cerebellum was pushed upward

Fig. 2 (case 1).—Median sagittal section of the brain. The tumor is infiltrated and enlarged by hemorrhage. There was also an extensive blood clot in the third ventricle which was removed before the photograph was taken.

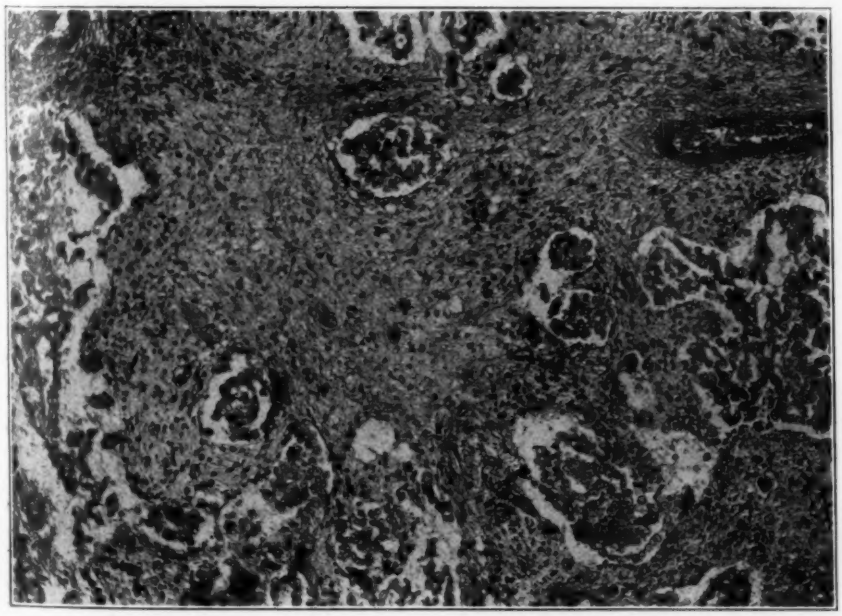

Fig. 3 (case 1).—Two types of tissue: (1) epithelial cells in clusters and (2) mesenchyme. Hematoxylin-eosin stain; × 80.

and backward and was very much flattened (fig. 2). The third ventricle was filled with blood clot, and the hemorrhage had evidently also infiltrated the tumor extensively and had spread around between the tumor and the bulb and cerebellum, showing that the tumor did not arise from these structures.

Microscopically the tumor was composed of two kinds of tissue, masses of epithelial cells and a stroma of connective tissue, carrying rather rare blood vessels (fig. 3).

The epithelial cells lay in anastomosing bands and masses, with frequent necrotic areas when they were too far from the vascular supply. The cells were irregularly

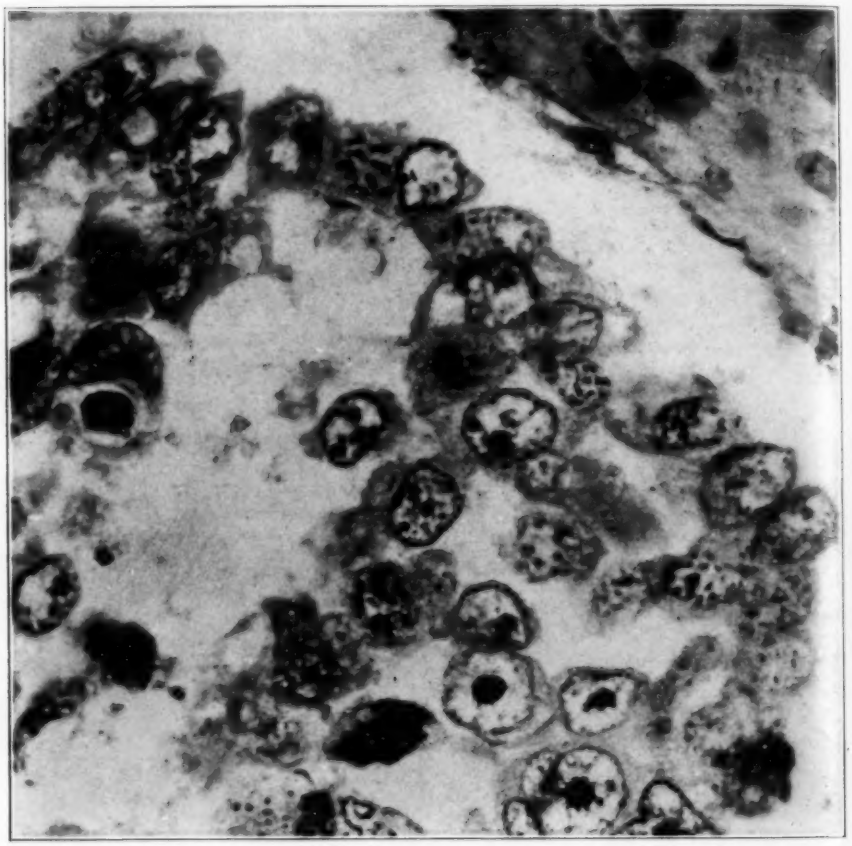

Fig. 4 (case 1).—Epithelial cells. Note the character of the nuclei, the presence of mitoses and blepharoplasten in the cytoplasm, particularly of one cell in the upper part of the photograph. Neutral ethyl violet-orange G; × 850.

polygonal, with abundant granular cytoplasm. Their nuclei varied greatly in size and shape but were uniformly vesicular. The chromatin granules were fine and tended to collect near the nuclear membrane. There was often a nucleolus of enormous size. In the cytoplasm might be seen often with ethyl violet-orange G stain a number of granules or short rods doubtless of the same character as those seen in normal cells of the pineal parenchyma. Many of the cells were multinucleated. Mitotic figures were numerous (fig. 4).

The stroma was of connective tissue, looking like primitive mesenchyme for the most part. The cells had little cytoplasm and formed numerous fine reticular fibrils. Their nuclei were small, oval or elongated, with a heavy nuclear membrane and rather dense chromatin network. There was some collagen around the blood vessels. Mitoses were occasionally found. In a few areas differentiation into cartilage was taking place (fig. 5).

Evidence of neuroglia was not found. Occasionally calcospherites were seen.

Comment.—Although the preceding observation might be considered to lend support to the view that destruction of the pineal body is responsible for the precocious development of puberty, it must not be forgotten that there exist observations of children in whom the pineal body was

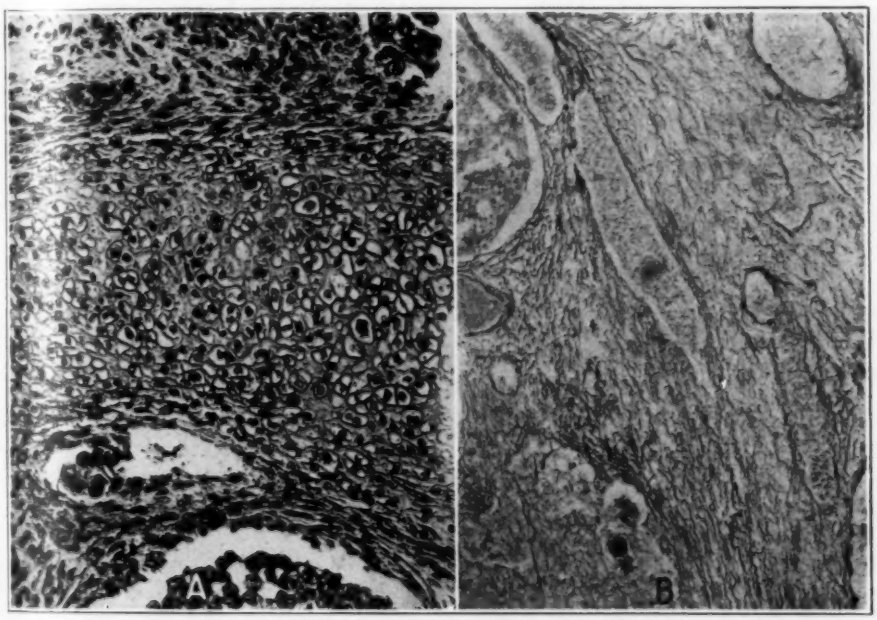

Fig. 5 (case 1).—*A* shows cartilage differentiating in mesenchyme. Phosphotungstic acid-hematoxylin; × 150. *B* shows only a few reticular fibrils differentiated in mesenchyme. Perdrau; × 100.

destroyed by a similar tumor and precocious puberty did not develop. Furthermore, in 1921, Klaproth [8] reported a case of pineal tumor associated with actual infantilism; in the same year, Zandren [9] recorded a case of infantilism in which no trace of the pineal body could be found at necropsy, although there was no tumor to distort the anatomic relations and the whole pineal region was cut in serial sections.

8. Klaproth: Teratom der Pineal combiniert mit Adenom, Centralbl. f. allg. Pathol. u. path. Anat. **32**:617, 1921.

9. Zandren: A Contribution to the Study of the Function of the Glandula Pinealis, Acta med. Scandinav. **54**:323, 1921.

Zandren was led by his case to suppose that the function of the pineal body was to initiate puberty. The preceding observation might be construed in such a way as to support this theory. The tumor found was a pinealoma, often called an adenoma of the pineal body. It might be argued that an adenomatous tumor, although destroying the pineal body, might still produce an exaggerated secretion and so cause the initiation of puberty. Unfortunately for this theory, not all the pineal tumors associated with pubertas praecox are pinealomas; many are teratomas, and one might point again to similar pinealomas unaccompanied by precocious puberty.

The following case fits in with neither the theory of increased secretion at puberty nor with that of decreased secretion. In this instance the

Fig. 6 (case 2).——Median sagittal section of brain, showing small flattened tumor of the pineal body.

pineal body was replaced by a malformation, and there is no evidence that any normal pineal parenchyma ever existed; yet the patient attained normal physical and sexual development.

CASE 2.—*Ganglioneuroma replacing pineal body. Pineal tissue entirely lacking. Normal physical and sexual development.*[10]

History.—E. R., a man, aged 40, was referred to the Peter Bent Brigham Hospital, Nov. 17, 1925, by Dr. Carl W. Rand of Los Angeles. The family and past histories were unimportant, the general physical mental and sexual

10. Previously mentioned briefly by one of us (Horrax), Arch. Neurol. & Psychiat. **17**:179 (Feb.) 1927.

development having been normal. Fifteen months before admission he began having headaches, which were usually frontal and were aggravated by coughing, sneezing and straining. Vision had failed for one year, the decline having been rapid during the four months prior to entrance to the hospital. Drowsiness had been a prominent symptom likewise for four months, and for the same length of time he had noted a marked staggering, progressing to inability to walk. During the three months prior to admission he had had two seizures associated with numbness of the right face, arm and leg. Recently he had had dysphagia and dysarthria.

Examination.—The patient was a well developed, normal appearing adult so far as general physical development was concerned. Pubic and axillary hair and external genitalia were of the fully developed adult type. The fundi showed bilateral choked disks of from 4 to 5 diopters. Although vision was considerably

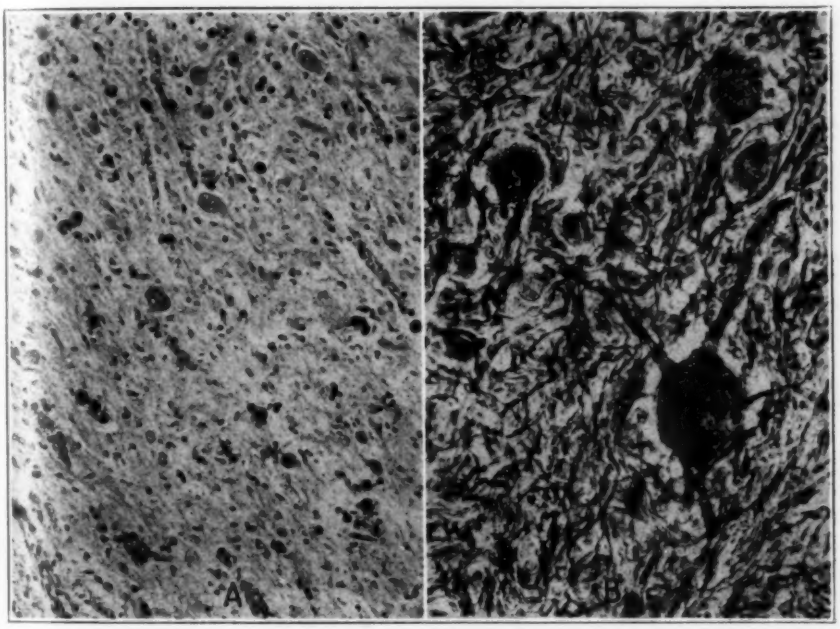

Fig. 7 (case 2).—*A* shows tumor composed of ganglion cells and others resembling those of an acoustic neurinoma. Hematoxylin-eosin stain; × 100. *B* shows ganglion cell with neurofibrils in processes. Cajal's reduced silver method; × 450.

reduced, he could still see large objects at a distance of 2 feet. The left pupil was larger than the right, and neither reacted to light. Conjugate movements of the eyeballs were impossible upward and downward, the lateral movements being normal. All deep reflexes were exaggerated bilaterally, with sustained clonus at both ankles and a positive Babinski sign on both sides. There were marked somnolence, dysarthria and dysphagia.

Course.—A diagnosis of pineal tumor was made, and on Nov. 20, 1925, Dr. Cushing performed a subtemporal decompression as a palliative measure. The patient died November 23.

Necropsy.—A complete examination was made thirteen hours post mortem. General examination revealed bilateral bronchopneumonia and an undescended atrophic testis on the right side. This testis did not give evidence of spermatogenic activity. The other organs were macroscopically and microscopically normal.

The brain was fixed in situ by injection of the carotid arteries with 10 per cent solution of the commercial solution of formaldehyde. No abnormalities of its external surface were to be seen. A median sagittal section passed through a small, flattened, circumscribed tumor of the pineal body, measuring on its cut surface 7 by 18 mm. (fig. 6).

Microscopically, the tumor was composed of scattered nerve cells in all stages of development, and between them were other cells of indifferent character. A

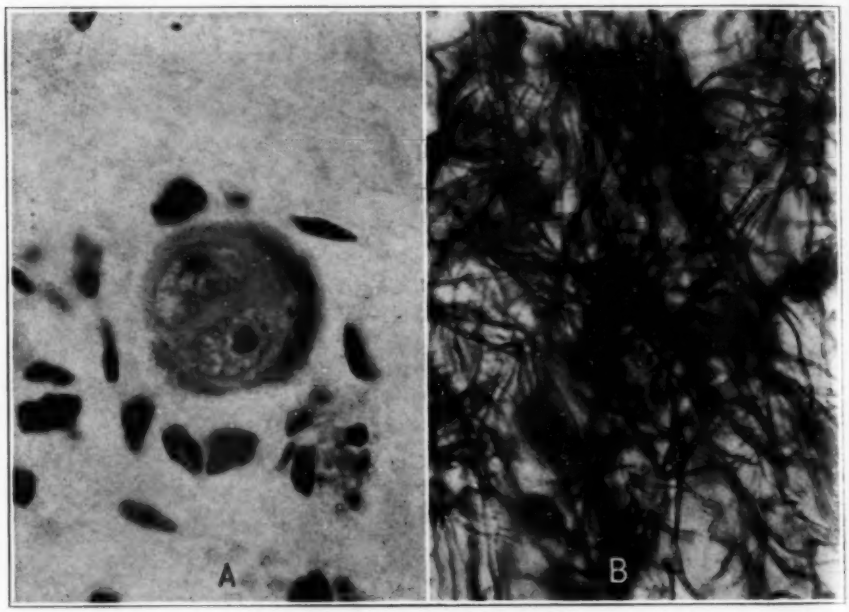

Fig. 8 (case 2).—*A* shows neoplastic nerve cell containing tigroid bodies. Bielschowsky-Plein stain; × 850. *B* shows area in which neuroglial fibrils are particularly numerous. Achucarro; × 850.

few small blood vessels were scattered about, and numerous calcospherites were present (fig. 7 *A*). The nerve cells were of all sizes and shapes, many of them multinucleated. They contained often, in the periphery of their cytoplasm, dustlike particles which stained with methylene blue, but rarely well formed Nissl bodies (fig. 8 *A*). The nuclei were large, spherical and vesicular, with one or two large nucleoli and little chromatin. Many of them had long, branching processes in which neurofibrils were impregnated (fig. 7 *B*). In the cell body, the neurofibrils were not clearly demonstrated. Myelin sheaths were not present.

The other cells of the tumor were probably to be considered as neuroglial. Most of them were bipolar, with oval nuclei having a delicate reticular network. Some were starshaped. Their processes were sometimes stained with ethyl violet and were better seen by Hortega's fourth variant or phosphotungstic acid-

hematoxylin (fig. 8*B*). Other interstitial cells had elongated heavily stained nuclei resembling those of the microglia. The method of fixation precluded their positive identification as such.

Nowhere were there any cells of the pineal parenchyma and nothing resembling the normal structure of the pineal body. The tumor was a typical ganglioneuroma.

Comment.—This case is interesting for many reasons. It is unusual that a typical ganglioneuroma should have been formed from the pineal

Fig. 9 (case 3).—General bodily configuration.

anlage. It has always been recognized that typical nerve cells are not found in the normal adult pineal body. Certain cells of the pineal parenchyma, however, have been considered by Krabbe [11] and others to be atypical nerve cells, although they recognized that tigroid substance and other distinguishing characteristics were absent. It is obvious from the preceding observation that the pineal anlage has a potentiality for

11. Krabbe: Histologische und embryologische Untersuchungen über die Zirbeldrüse des Menschen, Anat. Hefte. **54**:191, 1916.

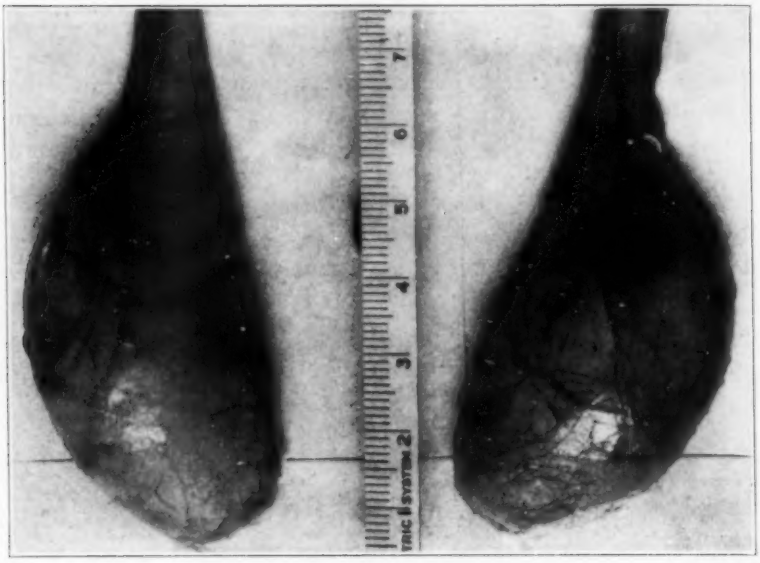

Fig. 10 (case 3).—Testes of adult size.

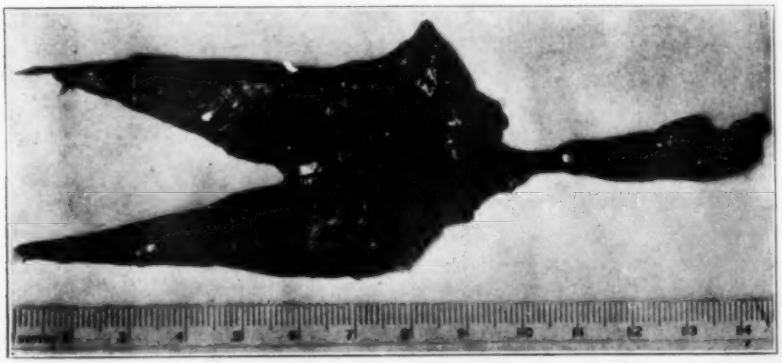

Fig. 11 (case 3).—Thymus gland (fresh).

developing nerve cells, whether or not this actually happens in normal development.

The small size of the tumor is also worthy of note. Pineal tumors have been conceived to cause precocious puberty by pressure on some hypothetical cerebral center. Certainly in this case the only pressure was on the tectum mesencephali which might account for the absence of pubertas praecox. The occasional infantilism accompanying pineal tumors may be explained as an effect of the resulting hydrocephalus, also absent in this case.

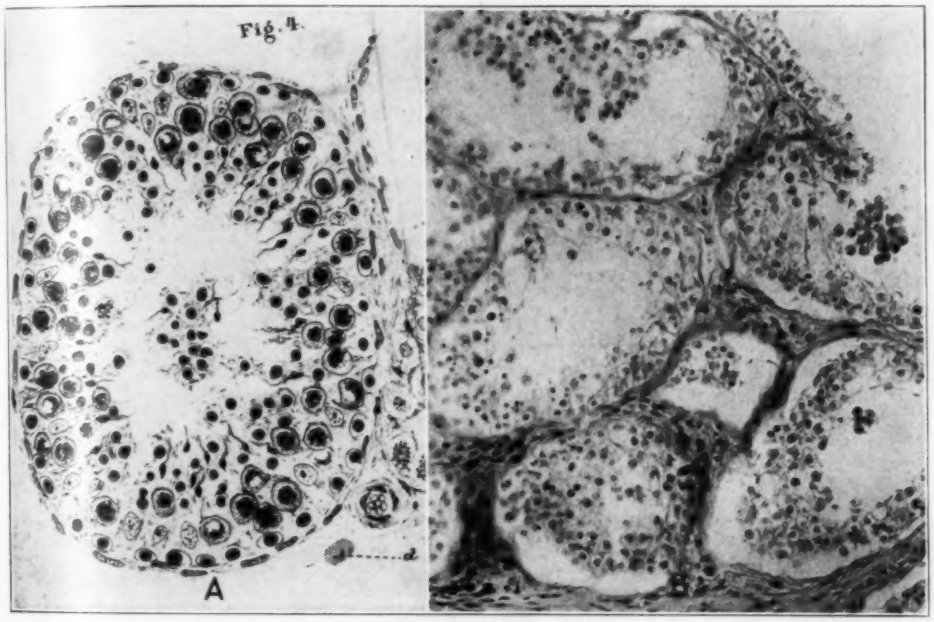

Fig. 12.—*A* shows testis of man, aged 42 years, after Spangaro. *B* shows testis of patient in case 3 showing corresponding stage of development.

It is interesting to speculate on the cause of death. There was no evidence of growth of the tumor, which must have been present for years. For some reason a block of the aqueduct of Sylvius must have occurred, and the obstruction might have been increased from edema caused by the decompressive operation.

Tumors of the brain apart from the pineal body may be associated with pubertas praecox. Such an observation was published in 1925 by Schmalz.[12] Our third case is similar, but even more striking. It is not

12. Schmalz: Ueber einen Fall von Hirntumor mit Pubertas praecox, Ziegler's Beiträge. **73**:168, 1925.

Fig. 13 (case 3).—Median sagittal section of brain. Amount and location of tissue removed at operation is clearly seen. Pineal body is in normal position, somewhat obscured by thickened meninges infiltrated with hemorrhage.

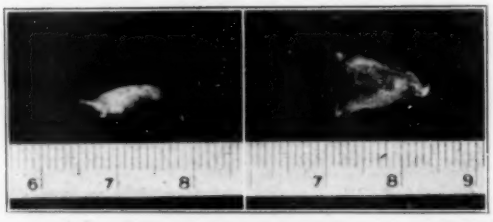

Fig. 14 (case 3).—Pineal body, lateral and upper surfaces.

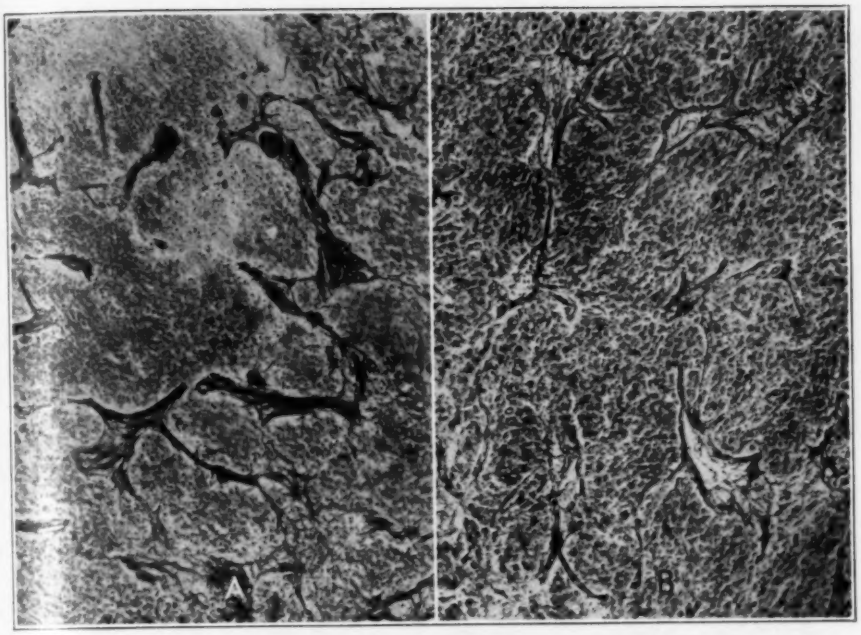

Fig. 15.—*A* shows specimen fixed in formaldehyde (case 3); Perdrau's method; ×80. *B* shows specimen taken from a control of the same age fixed in Zenker's fluid which accounts for difference in intensity of impregnation of the background. The architecture is identical in each case.

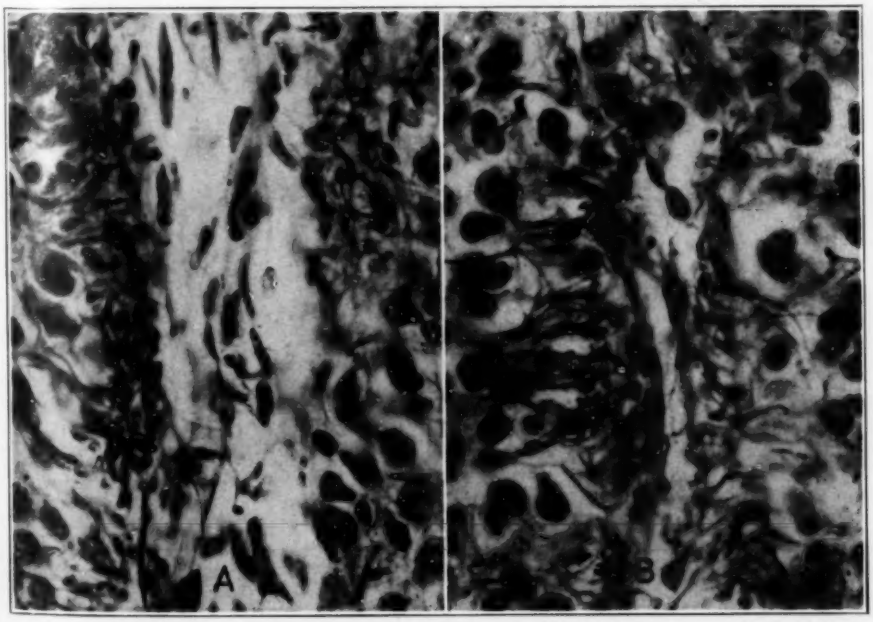

Fig. 16.—*A* shows specimen taken from control. *B* shows specimen taken from patient in case 3. Hortega's method for the pineal parenchyma; ×700. Note the rows of bulbous terminals of the cells of the pineal parenchyma in each case.

strictly an observation of pineal pathology but bears on the relationship of the pineal body to the syndrome of Pellizzi.

CASE 3.—*Outspoken pubertas praecox commencing at the age of 3 years. Large tumor of the third ventricle. Normal pineal body.*

History.—R. R., a boy aged 7, was referred to the Peter Bent Brigham Hospital on July 2, 1926, by Dr. P. H. Sylvester of Boston. The family history

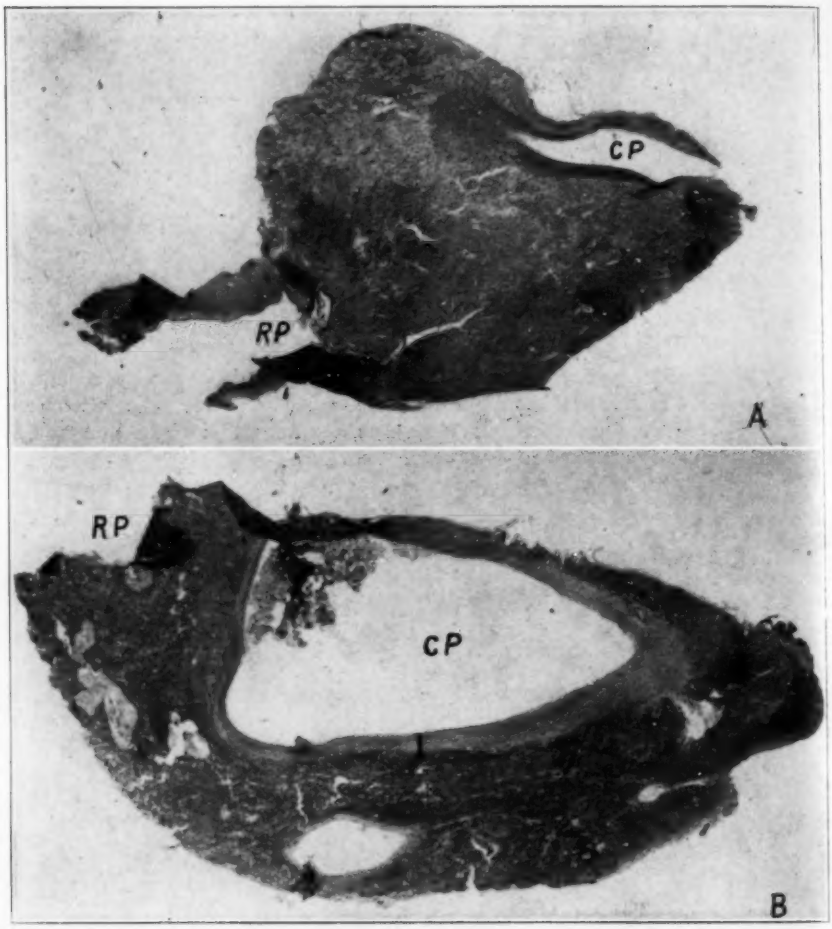

Fig. 17.—*A* shows pineal body from a child, aged 7 years (E. J.) with tumor of the brain and hydrocephalus but no pubertas praecox. *B* shows pineal body from patient in case 3. Achucarro preparations; × 11. *C. P.* indicates cavum pineale, and *R. P.* indicates recessus pinealis. The dorsal surface is up in each case.

was unimportant. The child weighed 7 pounds (3.175 Kg.) at birth. At the age of 3, he began to develop pubic and axillary hair, which within a year reached adult appearance. During the same year the external genitalia grew to adult proportions, and the voice assumed the deep, adult masculine tone. A generalized

adiposity gradually developed. He did not have any other particular abnormalities until one year before admission, when he developed a persistent internal squint of the right eye. For the month previous to admission, he had passed excessive amounts of urine daily, and for two weeks he had seen double.

Examination.—The child, as shown by the photographs (fig. 9) presented a most striking and completely mature appearance. The height was 56 inches (142 cm.), the average normal for his age being 44.1 inches (111 cm.). The weight was 110 pounds (50 Kg.), whereas the normal for this age is 49.5 pounds (22 Kg.). The general muscular development was of adult configuration, although there was, in addition, a distinct general adiposity. Axillary and pubic hair were present and showed no departure in type, distribution or abundance from that seen

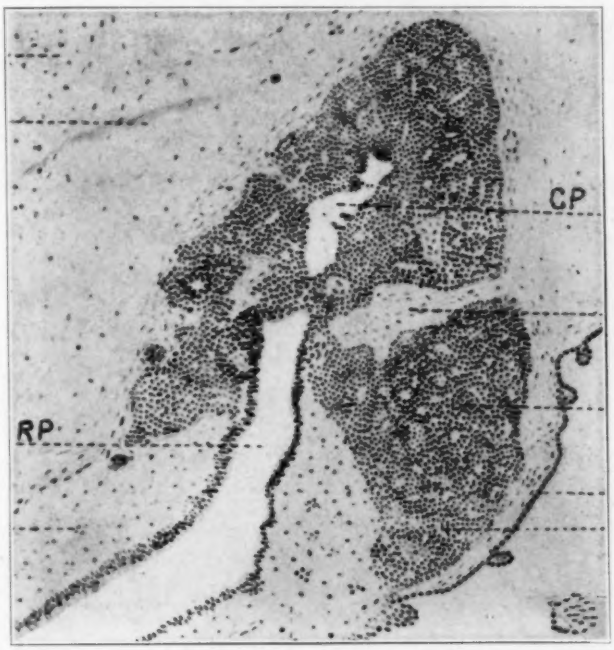

Fig. 18.—Pineal body of a fetus of 6 months, showing the manner of formation of the cavum pineale. *C. P.* indicates cavum pineale and *R. P.*, recessus pinealis. Copied from Krabbe.

in the normal adult male. There was also marked hirsutes of the thighs and legs generally. The voice was of the deep adult masculine type.

Neurologically he showed only a right abducens weakness and bilateral choked disks of 5 diopters. Roentgenograms of the skull showed an area of dense calcification above the sella turcica, slightly to the right of the median line. Roentgenograms of the hand and arm corresponded to those seen at 18 years of age.

Operation.—On June 23, 1926, a transfrontal exploration of the pituitary region was undertaken by Dr. Cushing. A puncture of the corpus callosum at this session revealed a tumor of the third ventricle. On July 1, 1926, this tumor was partly removed at a second operation, but the child died the following day.

Necropsy.—A complete necropsy was performed four and one half hours post mortem. The thyroid, thymus, suprarenal, hypophyseal, parathyroid and sexual glands were dissected out and photographed. They were all macroscopically and microscopically normal except the testes (fig. 10) and thymus (fig. 11). The latter seemed to contain more fibrous tissue and fat than is normal at this age. It weighed 12.5 Gm. The prostate gland was of adult type, but had no corpora amylacea. The other internal organs were normal.

The structure of the testes was that of a full grown man (fig. 12). Numerous spermatocytes, spermatids and spermatozoa were present. The interstitial cells occurred in small clumps; they looked like those of an adult except that they

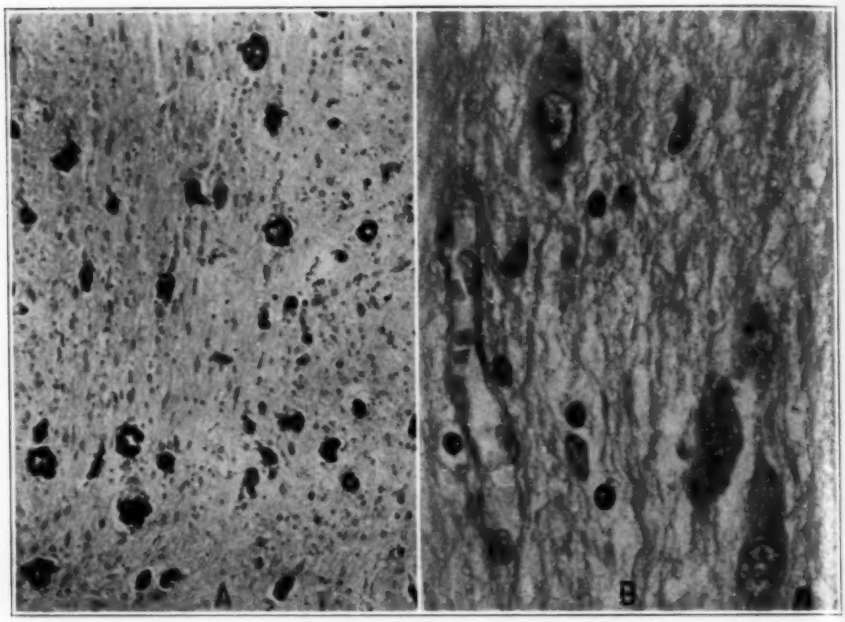

Fig. 19 (case 3).—*A* shows general structure of tumor. Hematoxylin-eosin stain; × 80. *B* shows large bipolar cells with vesicular nuclei. Hematoxylin-eosin; × 600.

did not contain pigment. Occasionally a mast cell was seen in the interstitial tissue.

Median sagittal section of the brain, which had been injected with 10 per cent solution of formaldehyde through the carotid arteries before removal, disclosed a solid tumor 4 cm. in diameter occupying the third ventricle and attached in the infundibular region (fig. 13). A considerable amount of its anterosuperior portion had been removed at operation. There was marked internal hydrocephalus. The pineal body was somewhat flattened and elongated, but of normal size (fig. 14). In its upper portion was a cystic cavity.

The structure of the pineal body was microscopically normal when compared with that of a boy of the same age (fig. 15). The cells of the pineal parenchyma

developed a normal number of bulbous terminations (fig. 16). The cyst proved to be a dilatation of the cavum pineale, normally present in the pineal body (fig. 17 *A*), arising as a constricted portion of the recessus pinealis of the embryo (fig. 18). The actual volume of pineal parenchyma may be seen, by comparison with another pineal body from a child of the same age (fig. 17 *B*), to be approximately normal.

Sections of the tumor were stained with hematoxylin and eosin, phosphotungstic acid-hematoxylin, Loyez, Bielschowsky-Plein, Cajal's reduced silver, Perdrau, Bielschowsky, Hortega's fourth variant and neutral ethyl violet-orange G. The tumor was made up of a great amount of fibrillary material running parallel in broad streams (fig. 19 *A*). Between the fibrils were scattered nuclei. The cells

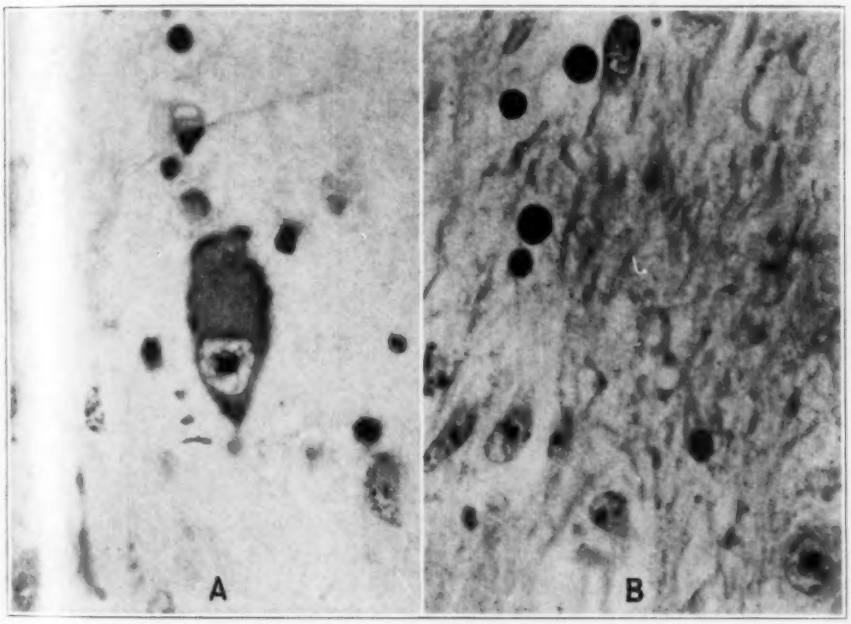

Fig. 20 (case 3).—*A* shows nerve cell with tigroid substance in periphery of cytoplasm. Bielschowsky-Plein stain; × 850. *B* shows poorly developed myelin sheaths. Loyez; × 850.

were usually fusiform, many of them with considerable cytoplasm (fig. 19 *B*). The latter cells had also larger nuclei which tended to be vesicular, with a heavy nucleolus and little chromatin. They could be shown to be neuroblasts, some unipolar, some multipolar, but mostly bipolar, for they contained Nissl substance (fig. 20 *A*) and gave origin to nerve fibers (fig. 21), many of which had poorly developed myelin sheaths (fig. 20 *B*). The neuroglial cells were also usually fusiform, but had less cytoplasm and smaller nuclei than those of the neuroblasts. They formed numerous neuroglial fibrils (fig. 21 *B*). The connective tissue was confined to the walls of the blood vessels, which had usually undergone hyaline degeneration and calcification.

The tumor must be classed as a ganglioneuroma.

Comment.—This case is practically a duplicate of the one of Schmalz, the patients in both cases having a large tumor in the infundibulum and a normal pineal body. The nature of the tumor in his case is not certain from his description, but it was probably some form of glioma.

The cyst of the pineal body was doubtless a dilatation of the cavum pineale, since it was surrounded by a thick layer of neuroglia. Berblinger, from an exhaustive study, says that these cysts of diverse origin which occur so frequently in the pineal body seem to have no effect on the bodily economy. It is not probable, therefore, that the

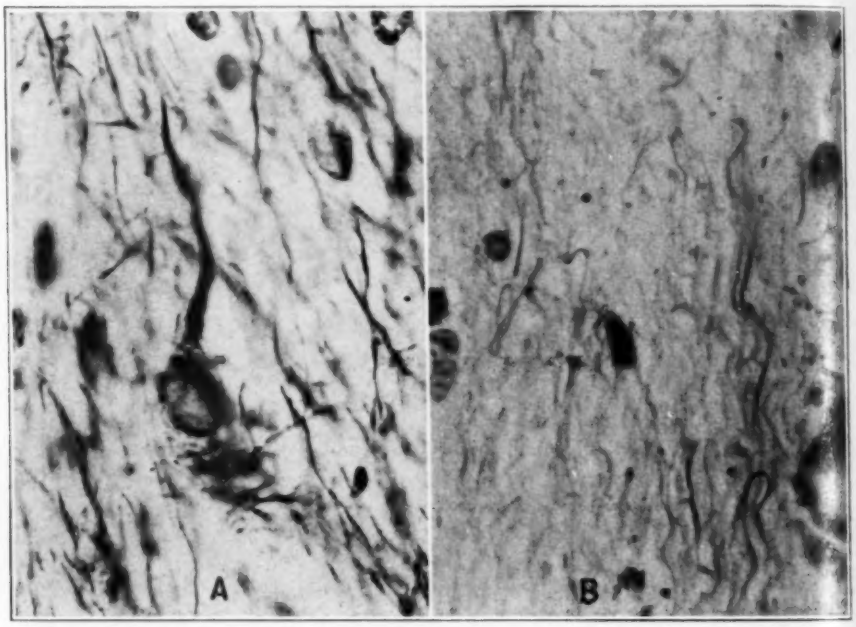

Fig. 21 (case 3).—*A* shows neuroblast. Cajal's reduced silver; ×850. *B* shows neuroglial fibrillae. Neutral ethyl violet-orange G; ×850.

syndrome of Pellizzi in this boy can be attributed to the pineal cyst, since a normal amount of microscopically normal pineal parenchyma was present.

The tumor was not a teratoma or a pinealoma, so that the syndrome cannot be attributed to a secretion furnished by the tumor. If we try to explain it by destruction of a hypothetical brain center, we are at once confronted by the numerous tumors in a similar situation unaccompanied by precocious puberty. Again we are left in the dark as to the essential cause of the macrogenitosomia praecox of which this boy was such an excellent example.

CONCLUSION

In reporting an interesting case of pinealoma which had spread widely in the subarachnoid space, Berblinger [13] remarked, "In the realm of the pathologic anatomy of the pineal body we must collect experiences and bring together observation after observation. With the increasing number of similar necropsy records, capable of being interpreted in the same manner without doing violence to the findings, our insight into the essential relationships will deepen." We submit these clinicopathologic observations as documents to be used in gaining this insight, being ourselves unable to interpret them in the light of our present knowledge.

DISCUSSION

DR. WALTER TIMME, New York: This interesting presentation by Dr. Horrax is somewhat surprising. In the first place, he arrives at the conclusion that the pineal body is in all probability not a glandiferous structure by exclusion negatively. Where would he place the following direct experimental evidence: (1) Tilney and Warren's exhaustive work on the pineal, which beyond any real reasonable doubt demonstrates glandiferous structure; (2) McCord's feeding experiments, in which by direct feeding of pineal substances directly to tadpoles rapid decolorization was obtained; (3) the counter experiment of Smith, in which these tadpoles after they have been decolorized, as it were, through the pineal, by the administration of anterior lobe of the pituitary regained their color rapidly; (4) the extirpation experiments of the pineal which produced enlargement of the testes of the experimental animals and an increase in their growth?

In his direct presentations, excellent as they are, his first case shows an actual change in the testis with an absolute pineal involvement. The second case, that of a man over 40 years of age, is without evidence of the presence of a pineal gland; at the age of 40 the pineal has involuted normally to a point of nonexistence. Krabbe and other investigators have shown that after the age of 20 the pineal practically disappears in a large majority of cases. No conclusion, therefore, can be derived from that. In the third instance, because the case happened to be one of pubertas praecox with a normal pineal body, he draws the conclusion that the pineal had nothing to do with pubertas praecox, a conclusion with which I agree. Practically all the cases of pubertas praecox are those that involve the suprarenal cortex, the interrenal gland, and time and again patients with cases of pubertas praecox have come to autopsy showing tumor or other disturbances of the suprarenal cortex.

Therefore, from the proof that he has advanced, I do not see that he is warranted in drawing the conclusion that the pineal is not glandiferous and that in the cases he has shown the evidence is absolute concerning that point.

DR. GILBERT HORRAX: I did not mean to draw any definite conclusions one way or the other about the pineal body. I simply stated that I was presenting these three cases for what they were worth, with the clinical evidence which they showed. In regard to the work by Tilney and Warren, it was my understanding that they found glandular elements only in the pineal body of lower animals and in the embryologic stage in human life.

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13. Berblinger: Zur Kenntniss der Zirbelgeschwülste, Ztschr. f. d. ges. Neurol. u. Psychiat. **95**:741, 1925.

The feeding experiments of McCord, with which I am familiar, showed not only the colorization changes but also an increase in the size of the animals to which he had fed pineal substance. That was why I said that so far as they went the feeding experiments controverted the evidence of extirpations; because in the extirpations also, such as have been positive at all (my own and those of Foa), the same thing has been shown; namely, an increase in the size of the patients and an increase in the size of their external genitalia. These two evidences are therefore contradictory.

Dr. Timme spoke also of my own experiments with extirpations of the pineal body in animals. There was a slight increase in the size of the animals, in some cases, and what I regarded as only a slight increase in the external genitalia.

Of the cases here reported, the first gave mild confirmation of the glandular theory of the pineal, because the boy, 9 years of age, with a pineal tumor had a slight increase in the histologic picture of the testes. The second case in a man aged 42 with a tumor replacing the pineal did not present any evidence, as this was a congenital type of tumor, that the man had ever had a pineal body. My understanding of Krabbe's work is that he absolutely denied the fact that there was any atrophy of the pineal at puberty.

In my last case, that of pubertas praecox with a tumor of the third ventricle, the other glands of internal secretion were normal, including the suprarenals, with the exception of the thymus, which was slightly enlarged.

MALIGNANT CHORDOMA OF THE LUMBAR REGION*

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AND
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The origin of chordomas in the chorda dorsalis has been definitely established. Virchow [1] was the first to describe such tumors and thought that he was dealing with cartilaginous formations. He termed these growths found at the spheno-occipital synchondroses "ecchondrosis physaliphora." Müller [2] first advanced the view that the tumor originated from the notochordal cells. His observations were not accepted definitely until 1895, when Ribbert [3] experimentally produced chordomas by puncturing anteriorly the intervertebral disks of rabbits. He thus definitely proved that chordomas originate from the notochord.

The histogenesis and the evolution of the tumors were first described in detail by Alezius and Peyron.[4] The clinical symptoms of the clivus were first noted by Klebs.[5] Fischer [6] was the first to describe malignant chordoma of the skull, and Mazzia [7] was the first to describe malignant chordoma of the sacrococcygeal region. A complete review of the subject has been dealt with by Stewart [8] and by Coenen.[9]

Tumors of the notochord are rare. Up to 1927, fifty-seven cases had been reported, twenty-seven of which originated at the clivus blumenbachii; twenty-eight at the sacrococcygeal region; one in the cervical region,[8] and one in the lumbar region.

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* From the Neuropathology Laboratory, Montefiore Hospital, New York.

1. Virchow: Untersuchungen über die Entwickelung des Schädelgrundes, Berlin, 1857.

2. Müller: Ueber das Vorkommen von Resten der Chorda Dorsalis bei Menschen nach der Geburt, über ihr Verhältniss zu den Gallertgeschwülsten am Clivus, Ztschr. f. rationelle Med., 1858, vol. 2, p. 202.

3. Ribbert: Ueber Ecchondrosis Physalifora spheno-occipitalis, Centralbl. f. Allg. Path. **5**:457, 1894; Ueber die experimentelle Erzeugung einer Ecchondrosis Physalifora, Verhandl. d. Kong. f. inn. Med. **13**:455, 1895.

4. Alezius and Peyron: Sur l'histogenèse et l'origine des chordomes, Compte. rend. Acad. d. Sc. **174**:419, 1922.

5. Klebs: Virchows Arch. f. path. Anat. **31**:369, 1864.

6. Fischer: Ueber ein malignes Chordoma der Schädelrueckgrats, Beitr. z. path. Anat. u. z. allg. Pathol., 1907, vol. 40.

7. Mazzia: Chordom der Sakralgegend, Zentralbl. f. allg. Path., 1910, vol. 21., p. 769.

8. Stewart: Malignant Sacro-Coccygeal Chordoma, J. Path. & Bact. **25**:40, 1922; A Review with Report of a New Sacro-Coccygeal Case, ibid. **29**:41, 1926.

9. Coenen: Das Chordom, Beitr. z. klin. Chir. **133**:1, 1925.

REPORT OF CASE

History.—R. I., a Jewish man, aged 64, born in Austria, was admitted to the Brooklyn Jewish Hospital, May 17, 1926, complaining of weakness and loss of control of both lower extremities which had persisted for the past ten months. The onset of the illness was in July, 1925, when he was confined to bed with attacks of vomiting and constipation. He also noticed great difficulty with the left leg in walking, with pain and stiffness in the thigh. About April 15, 1926, he experienced a peculiar sensation of numbness of both buttocks and thighs. He

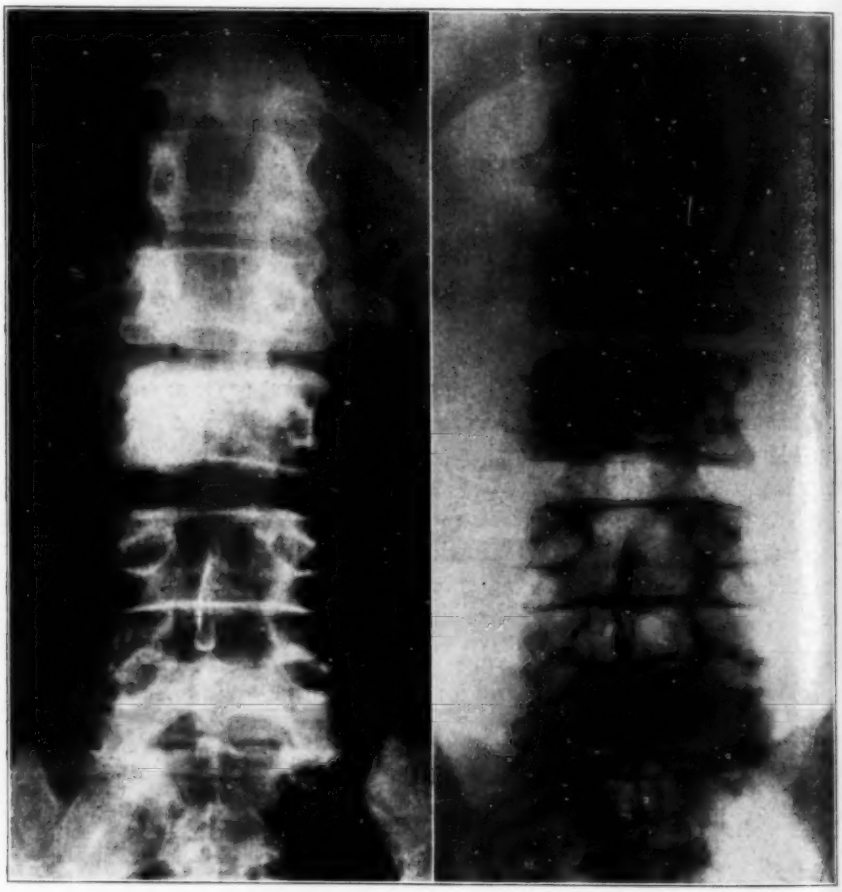

Fig. 1.—Roentgenographic appearance of the lumbar spine. Left negative and right positive, showing the "vertèbre d'ivoire" in the left half of the third lumbar vertebra.

was again confined to bed for five weeks and remained there until brought to the hospital.

Examination.—On admission, the upper abdominal reflexes were active and the lower diminished; the cremasteric, suprapatellar, patellar and achilles reflexes were absent; the Babinski sign was not present. Power was diminished in both lower extremities, and this was more marked on the right; atrophy of the muscles was not apparent.

Sensation: Vibratory and muscle sense were diminished in the left lower extremity; tactile sensibility was diminished on both lower extremities below the first lumbar dermatome, the loss being more marked on the left; pain sensibility was markedly affected on both sides, more on the left.

Spinal Fluid: The fluid was xanthochromic and contained 10 cells; otherwise, it was normal.

Diagnosis.—A diagnosis was made of tumor involving the lumbar segments of the cord or of a tumor of the cauda equina lying on the left side and anteriorly, involving especially the second, third and fourth lumbar vertebrae.

Fig. 2.—Posterior view of the spinal canal, showing tumor mass compressing the cauda equina.

Operation and Course.—The patient was operated on, June 4, 1926, by Dr. Elsberg, who found a tumor on the left of the cauda equina. He was discharged and admitted to the Montefiore Hospital, Nov. 25, 1926. On admission, he complained of incontinence of urine, constipation and weakness. Examination showed spasticity of both lower extremities, more marked on the right. The knee reflexes were diminished on both sides, more on the left; the achilles reflexes were absent on both sides. Positive Babinski, Oppenheim and Gordon signs were present on both sides. Definite atrophy of the gluteal, vastus and peroneal groups of muscles was found.

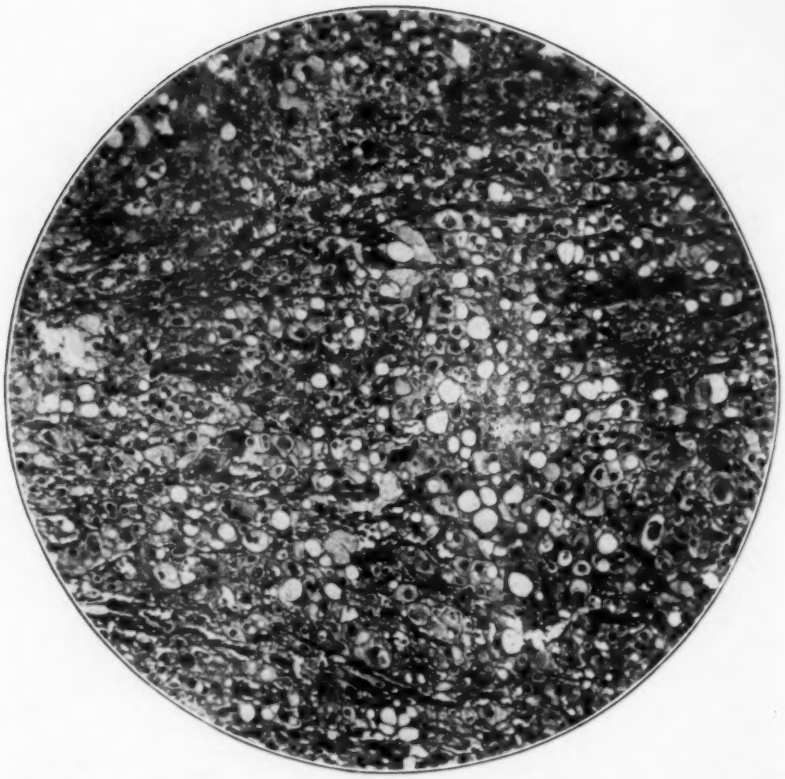

Fig. 3.—Cytologic structure of the tumor as seen after the first operation. Hematoxylin and eosin stain; Zeiss, 8 mm. aperture, compensating oculars, 10×.

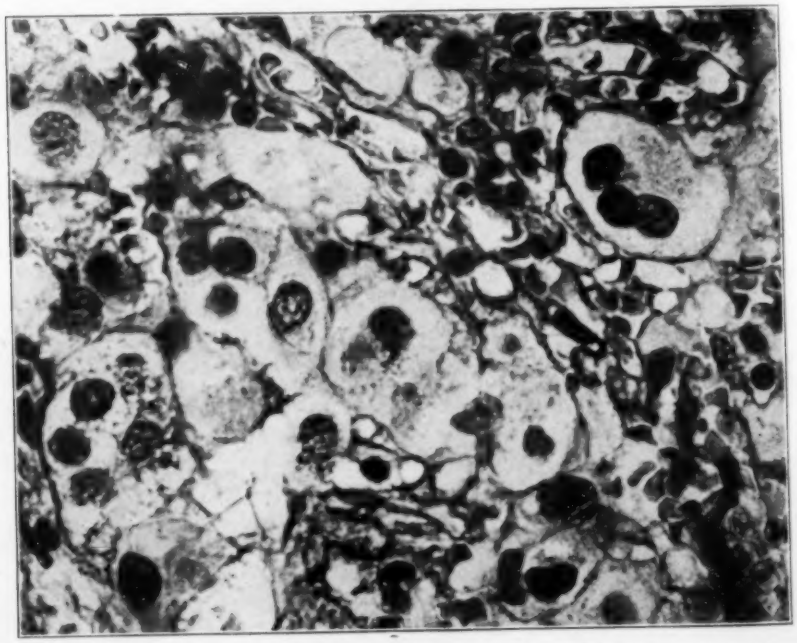

Fig. 4.—Enlargement of figure 3, showing large vacuolated polynuclear physaliphorous cells. Zeiss, 4 mm. aperture, compensating oculars, 10×. [Slide by courtesy of the Brooklyn Jewish Hospital.]

Vibratory sense was diminished below the first lumbar dermatome, with total loss of pain, temperature and touch sensation in the lowermost segments and hypalgesia above the first sacral segment. A diagnosis of tumor of the spinal cord was made. On Nov. 11, 1926, roentgen-ray examination of the lumbar spine showed marked sclerosis of the left half of the body of the third lumbar vertebra. The exact nature of the process in this vertebra could not be determined; it was suggested that it might be due to a neoplasm (fig. 1). Radium was applied, Jan. 7, 1927.

The patient died, January 31, of pneumonia.

Fig. 5.—Subdivision of tumor into lobules by connective tissue trabeculae. Del Rio-Hortega stain; Leitz objective 1, ocular, 1.

Necropsy.—Grossly, there was a tumor in the left lateral and outer surface of the spine between the third and fourth lumbar vertebrae. The mass measured 6 by 4.5 by 3 cm. The surface of the tumor was uneven and potato-like; it was firm in consistency and fibrous. The tumor was closely connected with the underlying vertebral arch and penetrated through the intervertebral foramen between the third and fourth lumbar vertebrae into the vertebral canal. The tumor was closely adherent to the bony tissue. By sawing the vertebral arch, the tumor was found to penetrate into the bone and into the disk between the third and fourth lumbar vertebrae. This mass was milky white, with disseminated glazy spots in the center. The appearance of the third lumbar vertebra differed from

the rest by its lighter color. Small masses, from 1 to 2 cm. long, were found within the canal (fig. 2) and showed the same characteristics as the main tumor but evidently were not in connection with the original mass. The cauda equina was compressed at this level (fig. 2). The meninges of the lower dorsal and lumbar regions were thickened. When the cord was cut at the upper lumbar region, the inner two thirds of the posterior columns showed a glazy appearance.

Histologic Report.—A section from the tumor obtained at the operation showed the typical picture of a chordoma: large vacuolated cells—"physaliphorous"—of

Fig. 6.—Arrangement of tumor cells in the periphery of the tumor. Van Gieson stain; Zeiss, 8 mm. aperture, compensating oculars, 10×.

epithelial aspect lying in a soft homogeneous basic staining matrix. Groups of polyhedral cells were also found (figs. 3 and 4).

Sections from the material obtained at autopsy showed an entirely different picture. The tumor was not uniform in character. The outer surface was covered by a thin layer of fibers of connective tissue from which trabeculae ran into the tumor tissue, subdividing it into lobules (fig. 5). Beneath the surface of this capsule, the tumor had a sarcoma-like appearance. The cells differed in size and form, and elongated spindle-shaped cells were intermingled with large polynuclear giant cells (fig. 6). Mytotic figures were frequently observed. Nearer the center of the tumor, the cellular masses were dissolved into a loose carcinoma-like network of polygonal cells embedded in a stroma, the character

Fig. 7.—Tumor cells in the masses found in the vertebral canal. Hematoxylin and eosin stain; Zeiss, 8 mm. aperture, compensating oculars, 10×.

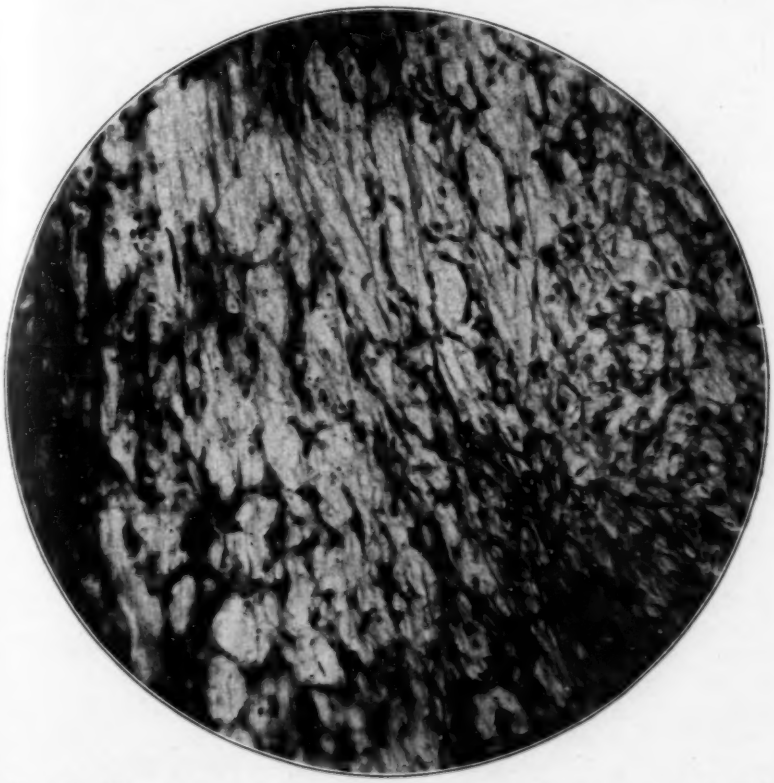

Fig. 8.—Myxomatous character and formation of numerous well defined fibrils. Hematoxylin and eosin stain; Zeiss, 16 mm. aperture, compensating oculars, 10×.

of which varied in different parts. In places, this stroma was formed by well defined thin fibers which stained intensively red with fuchsin; in other places, it was homogeneous in character, staining densely blue with basic dyes. The outlines of the cells in this area were well defined, and the nucleus was large and finely granular. Large polynuclear and physaliphorous cells of varying degree of vacuolization were intermingled with the polygonal cells.

The resemblance to the original tumor was more pronounced in the small tumor masses found in the vertebral canal. The histologic picture was more uniform in character than that of the main tumor, and closely resembled the material obtained at the operation (fig. 7). In the center, the tumor had a

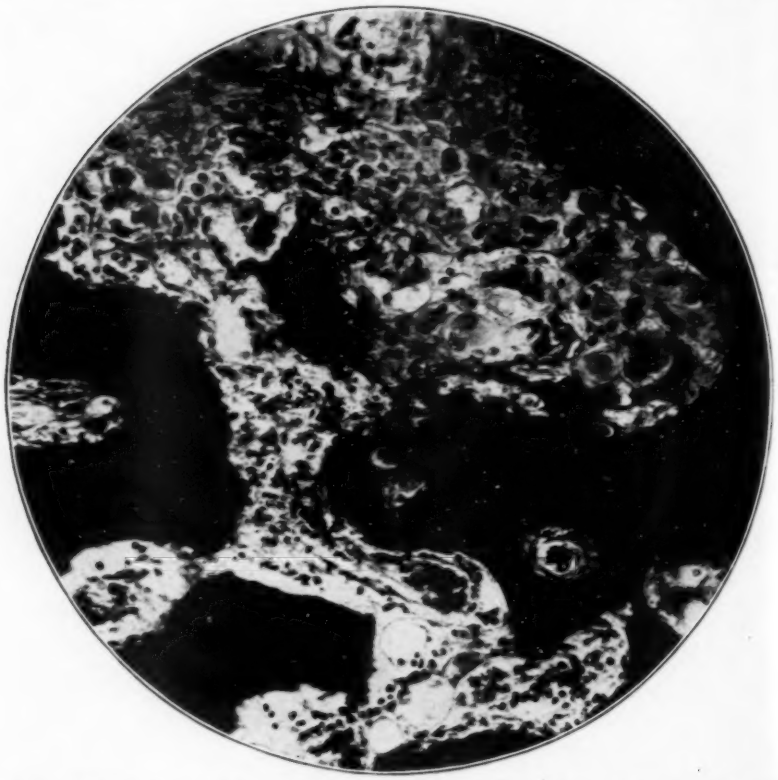

Fig. 9.—Invasion of the bone marrow by tumor cells. Van Gieson stain: Zeiss, 16 mm. aperture, compensating oculars, 15 ×.

myxomatous appearance. Numerous well defined fibers were embedded in the matrix (fig. 8), and spicules of bone were found. In other places, the tumor cells were seen to invade and cause destruction of the bone (fig. 9).

Sections of the spinal cord showed degeneration of the columns of Goll.

The character of the tumor in the outer layer placed it in the group of sarcomas. The character of the deeper layers and the arrangement of the cells showed its definite relation to the section obtained at biopsy.

The physaliphorous cells and the staining quality of the matrix characterized this tumor as a chordoma; the malignant condition of the tumor was characterized by invasion, destruction of bone and numerous mitotic figures.

Diagnosis.—The tumor was diagnosed as a malignant chordoma.

COMMENT

Most of the chordomas described were found at one or the other end of the original chorda dorsalis. Remains of the chorda dorsalis in adults are found in the nuclei pulposi of the intervertebral disks.[10] Ribbert produced chordomas by lesions of the nuclei; therefore, chordomas may occur at any segment of the vertebral column. However, of all the chordomas reported only four occurred at points other than the spheno-occipital and sacrococcygeal regions.

Chordomas are difficult to differentiate, according to Eckel and Jacobs [11] and others, from myxoid chondroma and colloid carcinoma of the intestinal canal. The case presented here showed difficulty in differentiation by its gross appearance and fibrous consistency. Usually, chordomas are soft and gelatinous in consistency, and clinically they are often mistaken for abscesses. The section obtained at the operation and the histologic appearance of the small tumorous masses of the vertebral canal aided in definitely establishing a diagnosis of chordoma.

It may be of interest to mention that the sclerosis of the left body of the third lumbar vertebra was found by the roentgen ray. Two photographs are given in figure 1. The first is a negative showing the left half of the third lumbar vertebra in white, the second is a positive showing the same in black. These types of changes in the vertebrae have been described before under the terms of "vertèbre d'ivoire" and "Marmorknochen." [12] They are occasionally found in patients with cancer of the breast and in others with tumors with metastases to the vertebral column. Their appearance is possibly due to an increase of calcium salts deposited in the vertebrae. The usual appearance of the vertebrae in cases of metastases is that of complete destruction and flattening. In this case, the vertebrae maintained their normal size and shape.

CONCLUSIONS

A case of malignant chordoma at the third lumbar vertebra is reported. This is the second case of its kind out of fifty-eight published case reports. The tumor differs from the classic chordoma by the fibrous consistency and the mixed character of the cytologic picture.

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11. Eckel and Jacobs: Malignant Spheno-Occipital Chordoma, J. Nerv. & Ment. Dis. **61**:471, 1925.

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LOCALIZATION IN ANIMALS OF STREPTOCOCCI FROM CASES OF EPIDEMIC HICCUP, ENCEPHALITIS, SPASMODIC TORTICOLLIS AND CHOREA *

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In a series of reports published in the medical literature during the last eleven years, I have emphasized [1] the importance in the etiology of diseases of the nervous system of certain streptococci having peculiar localizing power. The experimental results, while not always conclusive proof of etiologic relationship in each of the diseases studied, have furnished a good working hypothesis which already has led to a better understanding of the cause and management of the diseases studied.

In 1916, I reported [2] a series of experiments in which lesions in the spinal cord or brain of animals, characteristic in situation, were produced by the intravenous injection of cultures containing streptococci from atria of the infection in cases of multiple sclerosis and transverse myelitis. Similar experiments in cases of neuralgia and multiple neuritis produced instead lesions chiefly in the dorsal nerve roots and peripheral nerves, respectively, in a high percentage of animals inocu-

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2. Rosenow, E. C.: Elective Localization of Bacteria in Diseases of the Nervous System, J. A. M. A. **67**:662 (Aug. 26) 1916.

lated. These experiments suggested strongly that specific or elective localizing power of streptococci, inherent or acquired, must be an important factor in the production of various diseases of the nervous system, just as I had shown this to be the case in other diseases. The work led to the isolation of the pleomorphic streptococcus in epidemic poliomyelitis in the same year and, in 1921, to a study of the etiology of epidemic encephalitis.

In encephalitis it was found that intracerebral injection of small amounts of suspensions (in sodium chloride solution) of material expressed from tonsils, swabbed from the nasopharynx or aspirated from pyorrhea pockets, and of the corresponding primary cultures in broth, was more likely to produce characteristic symptoms than intravenous injection, and often served to separate the causative streptococcus from contaminating organisms and other streptococci which did not possess neurotropic power. By this method, the condition of profound lethargy never before seen or described in rabbits, together with other concomitant symptoms manifested by the patient, was produced with a streptococcus from a fatal case of epidemic encephalitis. In this case, the streptococcus was isolated from infected teeth, from the filtrate of the nasopharyngeal washings, from the blood during life, from an emulsion of the base of the brain after death and from a filtrate of the emulsion of the brain. It was demonstrated in the lesions of the brain and proved to be absent in the normal brain tissue. It was isolated from the brain and demonstrated in the lesions of positive animals. Similar experiments with material from normal persons failed to yield this organism. Since that time, similar results have been reported with culturally and immunologically identical streptococci in eighty-one cases of various forms of encephalitis. An agglutinating and curative serum has been prepared and used to identify suspected strains and in the treatment of a series of patients with encephalitis. The streptococcus isolated in these cases often varied greatly in size, depending on the medium in which it was cultivated. Exceedingly small forms were found, especially in old cultures in Noguchi's medium, and large, ordinary-sized, and exceedingly small forms were demonstrated in the lesions in a series of fatal cases of encephalitis by Rosenow and Jackson.[3]

Moreover, epidemic hiccup, that strange condition manifested by changes in character and posture, associated often with extreme respiratory arrhythmia that may follow attacks of encephalitis, spasmodic torticollis and chorea, has been reproduced, in the main, in animals with similar streptococci isolated from various atria of infection in these

3. Rosenow, E. C., and Jackson, G. H.: Microscopic Demonstration of Bacteria in the Lesions of Epidemic Lethargic Encephalitis, J. Infect. Dis. **32**:144 (Feb.) 1923.

diseases. The experiments with epidemic hiccup were especally illuminating. Spasms of the diaphragm were produced with great regularity, in rabbits, guinea-pigs, and monkeys (a condition not known to occur spontaneously in these animals) with cultures from the nasopharynx or tonsils in cases occurring in a series of outbreaks. It was found that spasms of the diaphragm could be produced not only after injection of the living streptococcus, but also when the organism was killed by heat or formaldehyde, and when corresponding broth-culture filtrates were used. After the living cultures had lost this power, the dead bacteria and filtrate also failed to cause diaphragmatic spasms. Likewise, filtrates of nasopharyngeal washings from patients at the time of the attack caused spasms of the diaphragm and of other muscles, while filtrates obtained after recovery and after the specific streptococcus had disappeared, were without effect.

Another striking example of the extreme specificity of the streptococcus and the variation in this property under certain conditions was found in experiments performed in a series of cases presenting varying degrees of neuromyelo-encephalitis which occurred during and after an epidemic of hiccup. Localizations, with lesions strikingly like those of the patient in situation, occurred in animals injected with material from the nasopharynx or tonsils. These results suggested strongly that the changing character in the epidemic was due to changes in the isolated streptococcus, since the symptoms and lesions in the experimental animal simulated so closely those of the patient in different stages of the epidemic.

A number of circumstances have retarded the general acceptance of the significance of these studies, especially in encephalitis, and reports on further studies are greatly needed. The work stood unconfirmed until recently, when Evans and Freeman[4] reported observations in several cases of epidemic encephalitis which in important respects paralleled those which I have reported. This is true especially as regards the site of isolation of the streptococcus, its sensitiveness to oxygen, its pleomorphism, filtrability and its effect in rabbits. The streptococcus isolated in these diseases morphologically and culturally resembles other streptococci which have only slight if any neurotropic properties. Hence, extraordinary proof of causal relationship is required. The streptococcus tends to lose specific localizing power on artificial cultivation as well as on successive passage through animals,

4. Freeman, Walter: Chronic Epidemic Encephalitis, J. A. M. A. **87**:1601 (Nov. 13) 1926. Evans, Alice C., and Freeman, Walter: Studies on the Etiology of Epidemic Encephalitis: I. The Streptococcus, U. S. Public Health Rep. **41**:1095, 1926. Evans, Alice C.: Studies on the Etiology of Epidemic Encephalitis: II. Virulent Bacteria Cultivated from So-Called Herpetic and Encephalitis Viruses, U. S. Public Health Rep. **42**:171, 1927.

and reproduction of the disease is thus rendered difficult. The streptococcus is highly sensitive to oxygen and may easily be missed. Emulsions of the brain in fatal cases may not contain a sufficient number of living organisms to affect animals, for it has been shown that if cultures or nasopharyngeal washings are too highly diluted, symptoms do not develop; this also has been well shown in the recent work of Evans and Freeman. The production of antibody is slight or not demonstrable, especially in afebrile cases, and hence agglutination or other serum reactions with suspected organisms are generally negative. Varying numbers of rabbits, the species of choice in these experiments, have been found to have spontaneous lesions of the brain resembling encephalitis. This objection, however, has been met in my own studies, because sections of the brain of numerous control animals showed the incidence to be very low (much lower than in the animals into which injections were made); the relation of the injected organism to the lesions was demonstrated microscopically, and similar lesions were produced in guinea-pigs, mice and monkeys, in which these lesions do not occur spontaneously. Moreover, the spontaneous disease is symptomless while, in my experiments, symptoms were pronounced and often simulated those in the patient from whom the strain was obtained. Because certain workers have succeeded in producing typical lesions in rabbits with virus and have isolated a small anaerobic organism resembling the globoid bodies of poliomyelitis, it is thought by many that streptococci cannot have etiologic significance. This contention, however, is no longer tenable, for Evans has recently reported the successful isolation of bacteria, including the streptococcus having neurotropic power, from the so-called viruses of encephalitis and herpes.

I shall now report further results on the localizing and symptom-producing power of the streptococci isolated in several diseases of the nervous system, and record the effects in animals of filtrates of broth cultures and nasopharyngeal washings.

The method of study was similar in the different diseases studied, and has been described in detail previously. It suffices to state here that the results summarized in tables 1 and 2 were obtained chiefly by injecting far forward into the right frontal lobe, from two to six rabbits, 0.1 cc. and 0.2 cc. of nasopharyngeal swabbings, or of pus expressed from tonsils suspended in 2 cc. of gelatin (0.1 per cent) Locke solution or these amounts of the primary cultures in dextrose brain broth, or of cultures from the apexes of extracted, devitalized teeth, diluted 1 : 10. Ether anesthesia was used in these experiments. Blood-agar platings were always made of the material injected to determine the viability and the kind of bacteria injected. The animals were observed as a routine twice daily and more often if active symptoms developed. In many instances, material from patients having a

different disease was injected on the same day into animals derived from a common supply; this served as a check on susceptibility of different breeds or lots. Exact dosage in this work according to weight or age, as in intracerebral injection of the virus of poliomyelitis in monkeys, is not essential.

TABLE 1.—*Mortality and Percentage Incidence of Symptoms in Animals Following Intracerebral Inoculation*

	Number of Strains	Number of Rabbits		Per Cent of Mortality	Spasms of Muscles			Abnormal Movements and Posture						Symptoms			
		Injected	Died		Diaphragm	Abdominal	Other	Nystagmus	Rhythmic Movements of Head	Tic-like Movements of Head	Ataxia	Turning of Head	Retraction of Head	Tremor	Hyperpnea	Paralysis	Lethargy
Epidemic hiccup	5	15	14	93	33	26	67	6	0	0	33	0	7	73	46	46	7
Epidemic encephalitis	9	50	37	74	2	2	10	4	0	0	20	2	6	34	24	48	54
Myoclonic encephalitis	6	31	21	68	3	3	52	9	0	9	23	3	3	55	42	26	9
Parkinsonian encephalitis	30	128	86	67	2	2	12	14	7	2	38	6	1	37	27	28	2
Respiratory arrhythmia	5	20	18	90	0	0	5	15	20	0	45	15	40	50	85	50	5
Spasmodic torticollis	16	52	31	60	0	8	23	12	8	15	44	19	27	27	33	19	0
Chorea	17	52	36	69	0	4	21	12	33	8	57	10	4	21	21	12	0

TABLE 2.—*Bacteria Isolated from Brain and Blood of Inoculated Animals*

Disease	Number of Animals Cultured	Brain or Blood	Bacteria Isolated				
			Green-Producing Streptococcus	Staphylococcus	Hemolytic Streptococci	B. Bronchisepticus	B. Coli
Epidemic hiccup	13	Brain	13	0	0	0	0
		Blood	7	0	0	0	0
Epidemic encephalitis	43	Brain	28	2	1	3	1
		Blood	17	3	1	4	1
Myoclonic encephalitis	20	Brain	13	1	1	0	0
		Blood	5	0	0	1	2
Parkinsonian encephalitis	93	Brain	58	11	4	4	2
		Blood	22	4	2	3	1
Respiratory arrhythmia	16	Brain	13	0	0	2	0
		Blood	2	0	0	2	0
Spasmodic torticollis	34	Brain	21	2	4	1	3
		Blood	15	1	2	1	1
Chorea	45	Brain	33	2	0	1	2
		Blood	24	2	0	1	1
Total	264	Brain	179	18	10	11	8
		Blood	92	10	5	12	6

CLINICAL RESULTS

There was no reasonable doubt as to the correctness of the diagnosis in the cases studied. Nearly all of the patients were seen in consultation with members of the staff of the Mayo Clinic and were considered as suitable for the possible isolation of the causative organism through intracerebral inoculation of animals with material from tonsils, throat or infected teeth. Definite evidence of focal infection was found in

most of the cases, and in some this evidence was marked, especially in the teeth. All of the cases in which inoculation of the animals was performed are included in tables 1 and 2, irrespective of whether the results were positive or negative.

In certain instances, the results in animals were used as evidence for or against the removal of tonsils or other foci of infection, although in most cases removal was advised irrespective of the laboratory results. Autogenous vaccines were prepared, in many cases, from the streptococcus isolated from the brain of animals with positive reactions. The clinical results from the removal of foci of infection and from the use of the vaccine in these and other cases will be reported later. Relief was obtained frequently in cases in which the symptoms had persisted for months, while in others a progressive course was arrested, and in still others apparent benefit was not evident.

The age of the patients ranged from 5 to 68 years in the different groups and was not of particular significance. The duration of symptoms in the cases of persistent hiccup ranged from two days to twenty-one months; in the group with epidemic encephalitis, from twelve days to five months; in that with myoclonus, from ten weeks to nine months; in that with the parkinsonian encephalitis, from one week to ten years; in that with respiratory arrhythmia, from six weeks to two years; in that with spasmodic torticollis, from six months to ten years, and in that with chorea, from two weeks to four months.

RESULTS OF EXPERIMENTS ON ANIMALS

The number of cases studied in the different groups varied from 5 to 30, the number of animals injected from 15 to 128, and the mortality rate from 60 to 93 per cent (table 1). The incidence of the different symptoms is recorded in percentages, hence the figures are directly comparable. In order to simplify the table, the fractions below 0.5 per cent are dropped, while the next higher figure is used if 0.5 or above. Certain symptoms, such as ataxia, tremors, hyperpnea and paralysis are relatively common in most of the diseases studied, especially in fatal cases, and, correspondingly, the general incidence of these symptoms is high in the experimental animals. Certain other symptoms, such as spasms of the diaphragm and abdominal muscles, lethargy, rhythmic and ticlike movements and rotation of the head, occur more rarely in patients affected with these diseases, and, in agreement with this fact, their general incidence is low in the animals that have received injections (table 1).

The incidence in the animals of the symptoms most characteristic of the different groups was often strikingly high, and in some cases simulated the condition in the patient so closely as to make one feel certain that the material injected must have contained the etiologic agent.

This occurred especially in cases in which the patients' symptoms were of recent origin or in which exacerbations of symptoms of long duration had occurred shortly before the study was made. Spasms of the diaphragm were noted in 33 per cent of all the animals injected with material from patients with persistent hiccup, which was in sharp contrast to the next highest incidence (3 per cent) of the symptoms in the other groups. Spasms of the muscles (67 per cent) was highest in the groups with persistent hiccup and in that with myoclonus (52 per

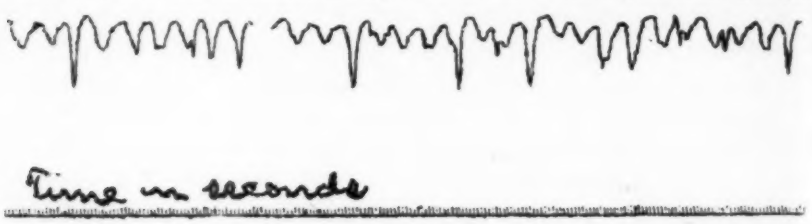

Fig. 1.—Curve showing spasms of the abdominal muscles in a case of myoclonic encephalitis of three months' duration. Note the spasms occurring irregularly at the end of inspiration.

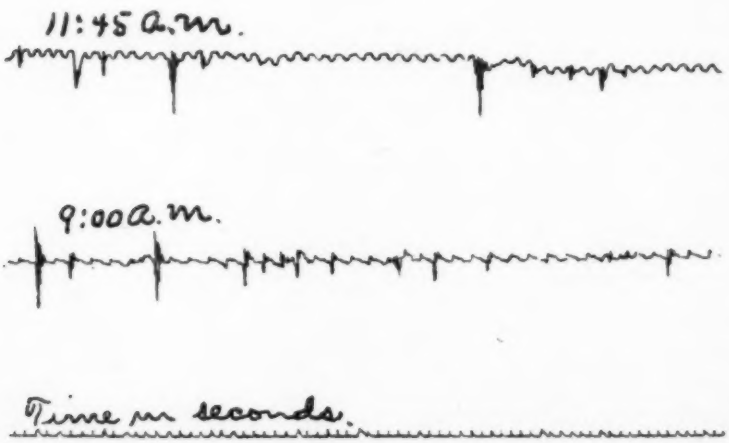

Fig. 2.—Curve showing spasms of the abdominal muscles in a rabbit injected intracerebrally, the day previously, with 0.2 cc. of a suspension from the nasopharynx in the case referred to in figure 1.

cent); it was also relatively high in the other two groups in which this was an outstanding symptom, namely, in spasmodic torticollis (23 per cent) and in chorea (21 per cent). In the cases of myoclonic encephalitis, the animals sometimes manifested spasms of the same group of muscles as was affected in the patient from whom the material was obtained (figs. 1 and 2).

As a prominent symptom, lethargy was noted in 54 per cent of the animals injected with material from patients with epidemic encephalitis;

this was in striking contrast to the next highest figure of 9 per cent in the groups in which this symptom was not encountered. It varied in intensity and duration from slight somnolence lasting for a day or two to deep sleep continuing for a number of days, from which the animal could be aroused only with difficulty. In one case of epidemic encephalitis, typical symptoms developed in all of four rabbits injected with material obtained directly from the tonsils and the nasopharynx and in all of three injected with streptococcus isolated from the brain of one of these. Moreover, the fresh filtrate of nasopharyngeal washings which yielded the characteristic streptococcus in cultures in dextrose-brain broth and meat-mash medium produced lethargy in both of the two rabbits injected. This symptom developed within several hours after injection, indicating the presence of a toxin having specific localizing or symptom-producing power. Cultures from the brain of these animals yielded the streptococcus, and emulsions injected directly into three other rabbits produced lethargic symptoms in two and encephalitis in all.

On the basis of these striking results, three additional rabbits were injected with the filtrate after it had been kept for four days in the ice box. All the animals remained well, and the cultures proved sterile.

The results in two additional cases of epidemic encephalitis studied at the same time were similar to those cited in the preceding case. Injections of suspensions of the pus from the tonsils of both patients produced lethargic symptoms of encephalitis in animals. The filtrate from a mixture of the suspension of the pus expressed from the tonsils, which proved sterile in culture, produced pronounced symptoms of lethargy in both of two rabbits given intracerebral injections. This began one hour after injection, continued for several days in both animals, and then disappeared.

In the group with parkinsonian encephalitis a particularly high figure was not noted among the symptoms listed in table 1, although ataxia (28 per cent) and tremors (37 per cent) were often pronounced. Slowness of movement, increased muscular tonus, rigidity in various regions and drooling of saliva, especially in animals that lived for some time, were not infrequently noted. The results in one case in this group, that of a patient with bulbar paralysis, manifested by weakness of the muscles of the tongue, throat and neck, were especially interesting. Two rabbits injected with the primary culture from an infected tooth of the patient and two with the emulsion of the brain of one of the rabbits injected with the primary culture manifested a bulbar type of paralysis beginning with weakness of the muscles of the neck. Three of four rabbits given injections with suspensions of the pus from the tonsils on two occasions, four days apart, also developed encephalitis.

manifested especially by weakness of the muscles of the neck, ears and fore extremities.

Hyperpnea and irregularity in breathing, often extreme, and sometimes associated with an expiratory grunt, were noted in 85 per cent and retraction of the head in 40 per cent of the animals inoculated with material from patients manifesting respiratory arrhythmia; this corresponded to the most striking symptoms noted in this group of patients. The results in one of these cases, that of a patient with extreme respiratory arrhythmia and hyperpnea, deserve special emphasis. Five of six rabbits injected with the undiluted and diluted (1:100) suspension of nasopharyngeal swabbings manifested pronounced respiratory symptoms and died, seemingly of bulbar paralysis. Cultures from the brain yielded the streptococcus in all. The strain from one of these rabbits was subcultivated rapidly three times and then grown in hormone broth for seven days. This exhaust culture was then filtered and the sterile filtrate injected intracerebrally into two rabbits, one receiving 2 cc., the other 1.5. The respirations became greatly increased in both, several hours after injection, but disappeared over night. Reinjection the following day produced hyperpnea as the chief symptom. Three days after the first injection, 7 cc. of the filtrate was injected intravenously in each of the rabbits; hyperpnea again appeared, lasted for several hours and then disappeared.

In sixteen cases in the spasmodic torticollis group, the symptoms induced were often strikingly like those characteristic of this condition in patients. Spasms of the muscles were noted in 23 per cent of the animals injected, ataxia, often extreme, in 44 per cent, ticlike movements of the head in 15 per cent, retraction of the head in 27 per cent, and turning of the head, due to tonic contraction of the cervical muscles, lasting often for weeks or months, in 19 per cent. The results with cultures from one of these cases of marked torticollis of six months' duration were most interesting. Symptoms developed in five of seven rabbits injected with suspensions of nasopharyngeal swabbings in dilutions as high as 1:1,000 and in two of three rabbits injected with material from infected tonsils. A filtrate from nasopharyngeal washings produced similar effects in two of three rabbits given injections, and heat-killed primary culture in seven of eight rabbits. Lethargy and hyperpnea were not observed. The similarity of patients' symptoms to those of the animals given injections was marked (fig. 3).

In the chorea group, ataxia, often extreme, was noted in 57 per cent of the animals given injections, rhythmic movements of the head in 33 per cent and spasms of the muscles in 21 per cent; these symptoms were in striking agreement with those commonly present in patients suffering from this disease.

Control inoculations with suspensions and cultures of streptococci without virulence or neurotropic power, sterile filtrates, sodium chloride solution, and broth, have been made in a large number of animals, always without apparent effect.

The incidence of the isolation of different bacteria from the brain and blood of the animals injected with material from patients in the different groups, and in which cultures were made after death, is given in table 2. Most of these died from the effect of the injection, although some were chloroformed for examination. The total incidence of the isolation of the green-producing streptococcus is much higher in each of the groups than of the staphylococcus, hemolytic streptococcus, *Bacillus bronchisepticus,* and *Bacillus coli.* Cultures from the blood yielded the streptococcus approximately only in one third of the animals from which cultures were taken, and hence the streptococcus was of

Fig. 3.—Turning and retraction of the head and attempts at their control in a patient with marked spasmodic torticollis of six months' duration.

low general virulence. Blood-agar plates usually showed a relatively small number of colonies of this organism and often no growth when inoculations in dextrose-brain broth yielded pure cultures. The number of colonies of the streptococcus from the brain on blood-agar plates was usually very large in the case of the animals that died soon after inoculation and very small in the animals that lived for a long time or that were anesthetized as they were recovering. Cultures from the brain were also frequently negative on blood-agar platings, when positive in dextrose-brain broth.

The green-producing streptococci isolated from the positive animals in the different diseases studied are very much alike morphologically and in cultural features, virulence and immunologic properties. The chief difference between the strains lies in their specific effects in animals on isolation, a property quickly lost, especially on aerobic cultivation.

The observations at necropsy were often largely negative and not characteristic of any of the diseases studied. Lesions at the point of injection were usually absent, although occasionally localized softening, with or without hemorrhage, was found. Suppurative meningitis almost never occurred, and when it did, it was nearly always due to hemolytic

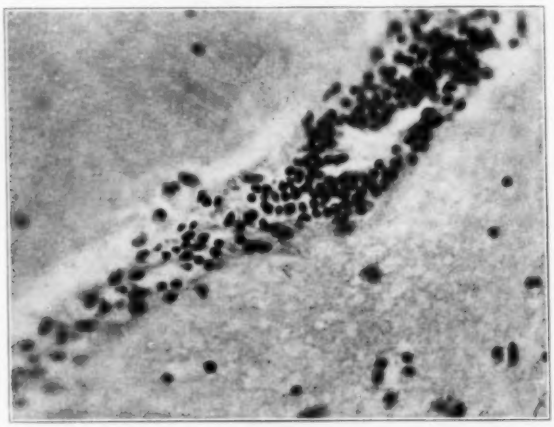

Fig. 4.—Typical perivascular, round cell infiltration in the midbrain of a rabbit injected, eleven days previously, with a suspension of the nasopharyngeal swabbings from a patient with typical lethargic encephalitis; × 250.

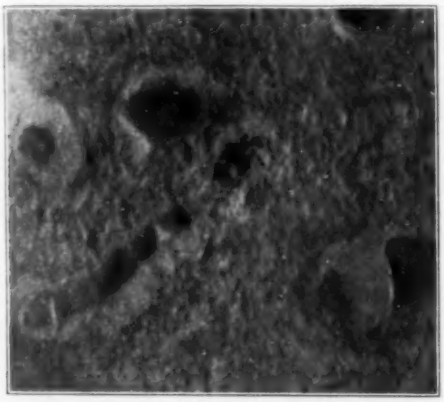

Fig. 5.—Streptococci in a perivascular space adjacent to the area of infiltration shown in figure 4; × 1,000.

streptococci. Moderate or slight clouding of the cerebrospinal fluid, clouding of the pia and congestion of the vessels of the meninges were found regularly in the animals that succumbed soon after injection but were rare in the animals that lived for a longer time. Gross hemorrhages into the pia or substance of the brain and spinal cord were rare and occurred most commonly in the medulla or pons following injection of

material from patients manifesting bulbar symptoms. Localized clouding and edema of the pia over the anterior aspect of the medulla, pons and cervical cord occurred especially in the animals injected with material from patients suffering from epidemic hiccup, spasmodic torticollis and respiratory arrhythmia. Besides edema of the lungs and infrequent dilatation and postmortem digestion of the stomach, lesions of the viscera were rare following intracerebral inoculation of material from different groups of cases. Lesions of the heart valves or endocardium, however, were commonly noted following intracerebral inoculation of the streptococcus from foci of infection or from the throats of patients suffering from chorea. This condition practically never occurred following inoculation of the streptococcus in cases of encephalitis and allied conditions. The microscopic changes produced were almost similar in the different groups and were characteristic in some of the diseases studied only as far as the site was concerned. Cellular infiltration varied greatly according to the duration of the experiment, size of dosage and virulence of the strain injected. Leukocytic and round cell infiltration of the pia was most marked surrounding the blood vessels in the sulci. Focal hemorrhages in the brain and medulla, often perivascular, associated with a variable degree of leukocytic and round cell infiltration, and similar areas of infiltration unassociated with hemorrhage, were usual observations in the animals that succumbed or were anesthetized during the first five days after injection. The streptococcus was readily demonstrated in these lesions. As the duration of the experiment became longer, hemorrhages were less common, the leukocytes were displaced by round cells, especially in the perivascular spaces in the midbrain (fig. 4), and the diplococci became fewer and more irregular in size (large and small forms often occurring side by side and sometimes in the same chain); they usually occurred in groups in perivascular spaces (fig. 5). The proportion of leukocytes and round cells varied greatly according to the site of the lesion; the former often predominating in the pia and the latter in the perivascular spaces in the depths of the brain substance.

Owing to the widespread presence of microscopic changes, or for unknown reasons, it was not always possible to correlate accurately the lesions found after death with particular symptoms noted during life.

COMMENT AND CONCLUSIONS

Another series of experiments with animals performed with material from foci of infection or throats of patients suffering from various diseases of the nervous system is reported. The results corroborate and extend the former observations. The streptococci isolated in each of these conditions, while much alike, possess very different localizing and symptom-producing power when injected intracerebrally into animals and readily lose this property, especially on aerobic cultivation.

The specific localizing power of the streptococcus, it would seem, is dependent, in part at least, on the production of a toxic or poison that has specific effects. Lethargy, hyperpnea with marked arrhythmia, and the symptoms characteristic of spasmodic torticollis have been produced with filtrates from nasopharyngeal washings, filtrates of suspensions of pus from tonsils and filtrates of old cultures of the specific streptococcus in each of these conditions. The fact that the streptococcus, having specific effects and the power to produce a specific poison, has been isolated long after onset indicates that the late manifestations of encephalitis and allied conditions are not sequels but are due to the activity of the causative organisms or its toxin, as has been especially emphasized by Freeman.

It is of course realized that the results obtained are not absolute proof of the etiologic relationship of the streptococcus isolated. None of the patients in this group died, and hence search for the organism in lesions could not be made. Agglutination experiments, especially with the serum of patients and the suspension of the suspected organism, while sometimes positive in low dilutions, were not so regularly enough to be convincing. The benefits which follow the removal of foci proved to contain the organism and the use of autogenous vaccines, while often striking, do not occur regularly enough to prove etiologic relationship.

In consideration of all the facts, especially the extremely specific effects obtained in some cases with the streptococcus isolated, and its specific toxin or poison-producing power reported herewith, the tentative conclusion seems warranted that this organism has etiologic significance in each of the diseases studied.

TUMOR OF THE BRAIN WITH WIDESPREAD METASTASES

A REPORT OF TWO CASES *

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In our experience in irradiation of tumor of the brain, comprising a series of 170 cases, there have been two unusual cases, details of which are reported in this article. In these cases widespread metastases developed, presumably from the brain lesion. Distant metastasis from a tumor of the brain is rare, and close study of the literature has failed to reveal a single reported case. We have felt considerable hesitancy, therefore, in reporting these cases as tumors of the brain with evidences of metastases, especially since we do not have one important link in the chain of evidence, a postmortem examination. If we are entirely wrong in our assumptions, however, and the cases are examples of primary brain lesions with coincident metastatic tumors of undetermined origin, they are still of scientific value.

REPORT OF CASES

CASE 1.—*History.*—Mrs. S. A., aged 41, was admitted to the service of Dr. Charles H. Frazier at the University Hospital on Feb. 13, 1914, with a complaint of constant occipital headache. She had had an operation five years previously at another hospital; a record of what was done at this operation could not be obtained. The patient had been well until eight months previous to admission, when she developed symptoms which were clearly those of cerebellar disease. Careful examination, including a roentgenogram of the head, which showed rarefaction of the skull over the posterior fossa on the right side, led to a diagnosis of cerebellar tumor. A suboccipital craniectomy revealed a large, hard, lobulated tumor practically filling the entire posterior fossa on the right side.

Treatment and Course.—The tumor was wholly encapsulated and firmly fixed; its exact origin could not be determined. A specimen was removed (fig. 1), and a pathologic diagnosis of endothelioma was made. Two weeks later, about three fourths (50 Gm.) of the tumor was removed by a second suboccipital craniectomy, and a diagnosis of endothelioma was made from the pathologic examination.

Roentgen-ray therapy, detailed in table 1, was instituted twelve days after the second operation. Following the operation and the roentgen-ray treatment, the patient improved remarkably and was almost entirely free from symptoms, with the exception of a slight awkwardness in gait. She was discharged from the hospital four months after admission, returning a year and a half later for

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* From the Roentgenological Department Hospital of the University of Pennsylvania.

radium treatments (table 1). At this time, there was no recurrence, and the radium was given as a precautionary measure. One year later, the patient was still in apparently good health, except that she sometimes had headache, and she remained well until two years later (1918), when the symptoms gradually returned, necessitating readmission to the hospital in June, 1920.

A roentgen-ray examination of the head at that time showed some atrophy of the posterior clinoid processes as the only evidence of tumor. A suboccipital craniectomy was performed, and a large encapsulated tumor of the cerebellum was found. Fifty milligrams of radium was implanted in the growth and allowed to remain for eighteen hours (table 1). Following discharge from the hospital a

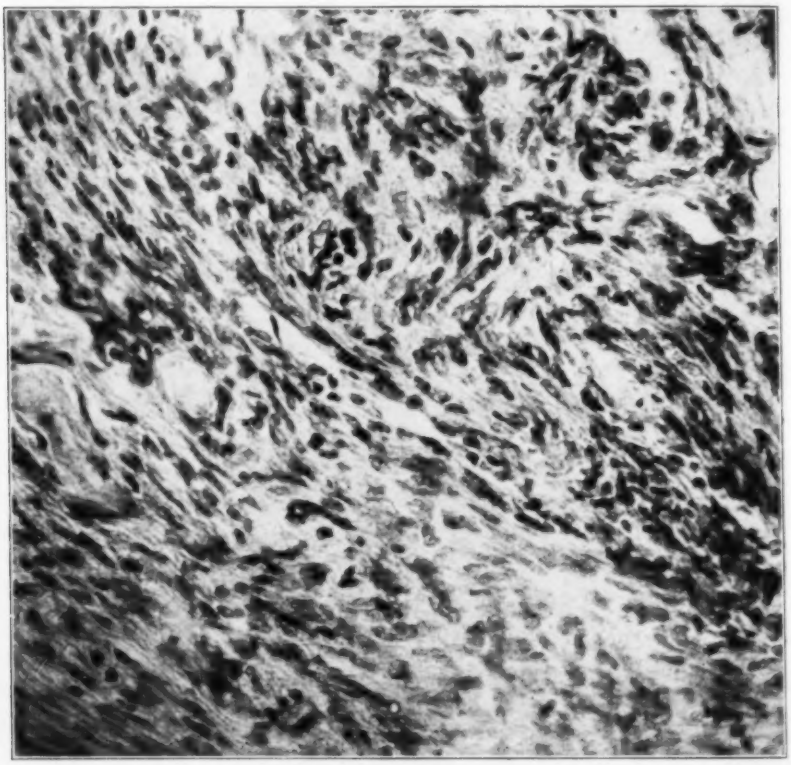

Fig. 1 (case 1).—Photomicrograph of the tumor which was diagnosed an endothelioma.

month after the operation, the patient received several series of radium treatments, extending over a period of three years. Shortly thereafter, deep roentgen-ray therapy over the back of the head was started, and she received three treatments at that time. Following this, the patient remained in about the same condition. She was admitted to the hospital several times for study and also received deep roentgen-ray therapy again in 1925. At that time, she complained only of occasional left frontal headaches.

A year later, on Aug. 2, 1926, the patient's physician telephoned to say that the patient was greatly improved, but on Aug. 17, 1926, she was admitted to the medical service of the hospital in an extremely serious condition; this was the

last admission to the hospital. Besides the former neurologic symptoms, the patient showed considerable weakness, emaciation, cough and diarrhea. This condition had started during January, 1926, with a dry cough, which had been unproductive and not accompanied by hemoptysis. The patient had lost 35 pounds (15.9 Kg.) in weight during this time. By June, she had developed symptoms of cardiac decompensation, and, about this time also, a persistent diarrhea and anorexia. Physical examination revealed, in particular, markedly engorged vessels on the left side of the neck, rapid respiration and prominence of the posterior portion of the left side of the chest, over which fremitus and breath sounds were decreased and the percussion note was dulled. In the left upper part of the abdominal region, a mass extended from under the costal margin to the level of the umbilicus, and from the flank half way to the midline. This did not move with respiration, and as it was dull to percussion and as its surface was slightly irregular, it was thought to be a metastasis. Roentgen-ray examination of the

TABLE 1.—*Irradiation Therapy of Patient in Case 1*

Radium Treatment								
Date	Mg.	Time	Filter	Dist.	Portals	Mg. Hours	Location	Method of Application
1915								
12/ 7 to 12/29	90	72 min.	2 mm. aluminum	½ cm.	31	110	Over occiput	Block
1920								
6/23	50	18 hrs.	4 mm. platinum	Implantation	1	900	Growth	Implantation
10/29	125	55 min.	2 mm. aluminum	½ cm.	49	110	Over occiput	Block
1921								
4/ 1	110	45 min.	2 mm. aluminum	½ cm.	45	82	Over occiput	Block
1922								
1/14	125	40 min.	2 mm. aluminum	½ cm.	30	82	Over occiput	Block
12/ 8	125	55 min.	2 mm. aluminum	½ cm.	15	110	Over occiput	Block

Roentgen-Ray Treatment								
Date	Time, Min.	Mill.	Kilovolt	Filter	Focal Distance, In.	Portals	Milli-ampere Minutes	Location
1914								
3/19 to 6/23	10	5	?	3 mm. aluminum	10	41	50	Over head
1923								
12/17	75	4	200	1 mm. aluminum 5 mm. copper	50	1	300	Over cerebellar region
1925								
10/21	75	4	200	1 mm. aluminum 5 mm. copper	50	1	300	Over cerebellar region

chest (fig. 2) showed advanced involvement of both lungs, probably from the endothelioma of the cerebellum. Roentgen-ray examination of the head at this time, however, did not show any metastatic involvement.

The patient was discharged as hopelessly ill, and she subsequently died at home, during the same month, August, 1926. Autopsy was not performed.

CASE 2.—*History.*—Miss L. K., aged 32, was admitted to the service of Dr. Frazier at the University Hospital on Nov. 1, 1919, her chief complaint being staggering in gait. The symptoms, which indicated cerebellar dysfunction and increased intracranial pressure, began about July of that year. The past history had been without significance, and there was nothing of interest in the family or social history. Physical and neurologic examinations at that time gave evidence of a cerebellar lesion.

Treatment and Course.—A first stage suboccipital craniectomy was performed several days after admission. Subdural tension was extreme, but on account of

the poor condition of the patient, the second stage of the operation was delayed for two weeks. At that time, the tension had subsided somewhat, and the only abnormality encountered was a somewhat larger right cerebellar hemisphere. The wound was closed, and the patient was subsequently discharged in about the same condition as on admission. A month later, the patient was readmitted, and an operation was again performed. A tumor was not found, but 50 mg. of radium was inserted in the left cerebellar hemisphere and left there for eighteen hours. Two weeks later, the patient was discharged in a fair condition. A pathologic

Fig. 2 (case 1).—The roentgenogram was made with the patient in bed because of weakness. It demonstrates metastatic involvement of both lungs.

report of a small amount of tissue removed proved it to be edematous cerebellar tissue.

During the next year, the patient remained about the same, but owing to an increase in symptoms, she returned to the hospital in January, 1921. Another operation was performed, and this revealed a large, soft, friable, grayish-red tumor covering the left cerebellar hemisphere. As much of this as possible was removed, and 50 mg. of radium was applied for eleven hours. Subsequently, the patient received five radium applications as detailed in table 2. The pathologic

diagnosis was glioma (fig. 3). The patient's condition did not improve, and she was discharged a month later with marked cerebellar symptoms. Five months after discharge, she returned for more radium applications and at that time did not seem so well as previous to the operation. However, she had neither headache nor pain. For approximately half a year, the condition remained about the same, and then the patient developed pain over the sacrum and also shooting pains in the legs. She did not return to the hospital, however, until a year and a half after these symptoms started.

On admission, in October, 1923, the symptoms were severe and accompanied by persistent edema of both legs, which had been present for several months, also pain in both shoulders, and emaciation. Whereas physical examination had previously given negative results, except for the neurologic observations, the patient now was emaciated, in much pain and appeared to have a malignant cachexia. There was a visible and palpable mass, just above the left buttock over the sacro-iliac joints, and the back in the lumbosacral region was discolored. A gynecologic examination gave negative results. Examination of the rectum revealed severe pain and tenderness in both sacro-iliac joints. A chordotomy was recommended because of the severe pain. At this time, a roentgen-ray examina-

TABLE 2.—*Irradiation Therapy of Patient in Case 2*

	Radium Treatment								
Date	No. of Tubes	Mg.	Time	Filter	Dist.	Portals	Mg. Hours	Location	Method of Application
1920									
1/30	1	50	5½ hrs.	1 mm. silver	Implantation	1	275	Growth	Implantation
1921									
1/22		110	1 hr. each	2 mm. aluminum	½ cm.	23	110 each	Over occiput	Block
2/24		125	45 min. each	2 mm. aluminum	½ cm.	18	94 each	Over occiput	Block
8/19		50	11 hrs.	1 mm. silver	Implantation	..	550	Into growth	Implantation

tion of the pelvis (fig. 4) showed evidence of an extensive growth involving both iliac bones, the right side of the sacrum, and probably beginning in the upper parts of the right femur. On examination of the lower part of the thoracic region and chest (fig. 5), confirmation was obtained of the previous observations of a large shadow to the right and in front of the spine and behind the heart. This shadow rose a considerable distance above the diaphragm, did not move with respiration and did not pulsate. Evidence of spinal involvement in this region was not present. A chordotomy was performed at the fifth thoracic level. Following this, the patient still had much pain and required morphine for relief. The morphine did give relief, however, although it had not done so previous to the chordotomy. Three weeks later she was discharged from the hospital. At that time, there was little pain in the legs, although some pain was still present in the region of both hips. The patient was to return for observation in two months, but died at home in the interval. Postmortem examination could not be obtained, and, unfortunately, we have not a record of the manner of death.

COMMENT

The patient in case 1 was one of the first we treated by irradiation. She always responded well but was never entirely relieved of symptoms by the irradiation. The lesion was a cerebellar tumor, the final patho-

logic report being endothelioma (fig. 1). The patient was operated on twice and had radium implanted into the growth once. During the summer, 1926, she developed metastatic lesions in the lungs and died in August, 1926. Autopsy was not performed.

An endothelioma of the brain is a malignant growth that tends to destroy and recur. Endotheliomas elsewhere in the body are prone to metastasize. In the case reported, the growth was exposed and partially removed twice, with the implantation of radium on one occasion.

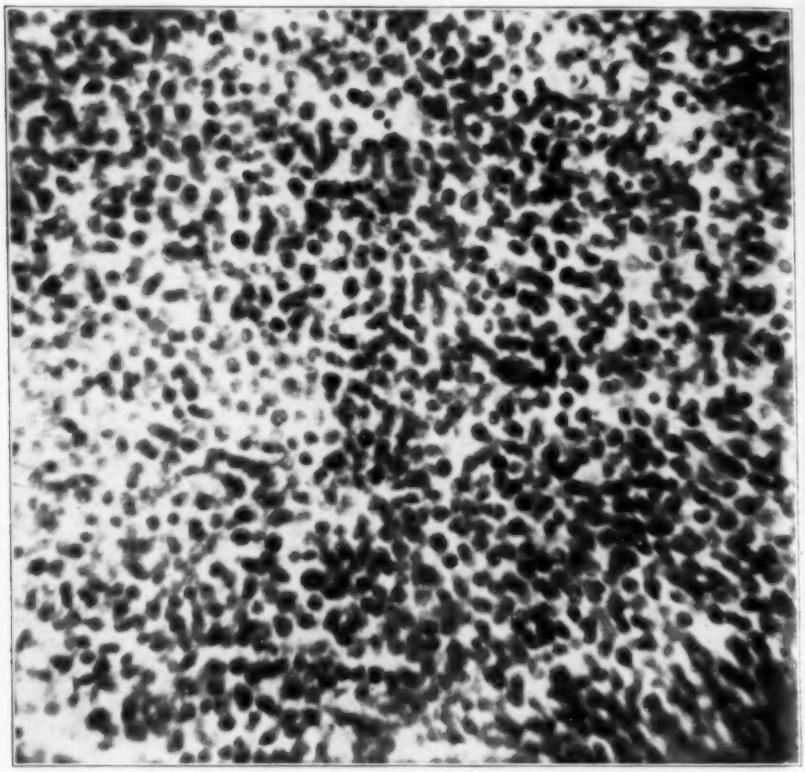

Fig. 3 (case 2).—Photomicrograph of tumor which was diagnosed glioma (medullary blastoma).

It is a common surgical experience for metastasis to occur in endotheliomas located elsewhere and treated by repeated operative procedure and irradiation.

In case 2, also a case of cerebellar tumor, the final diagnosis was glioma (medullary blastoma). This type of tumor is also a malignant and cellular growth. The patient was operated on four times, with radium implantation twice, the growth being traumatized frequently. The growths in the chest and on the back near the sacrum, with metastatic involvement of the pelvis, could not be accounted for by

the discovery of a primary tumor elsewhere than in the brain. The patient died on Jan. 1, 1924, but autopsy was not performed.

LITERATURE

The metastasis of tumors of the brain to various portions of the central nervous system and to the pia has been recorded in the literature several times, but metastasis to other parts of the body has not been reported. Spiller [1] quotes Borst,[2] who says that metastasis of glioma is exceedingly rare, and, in fact, adds that multiple gliomas had not been positively observed up to that time (1921). In a case of Stroebe's,

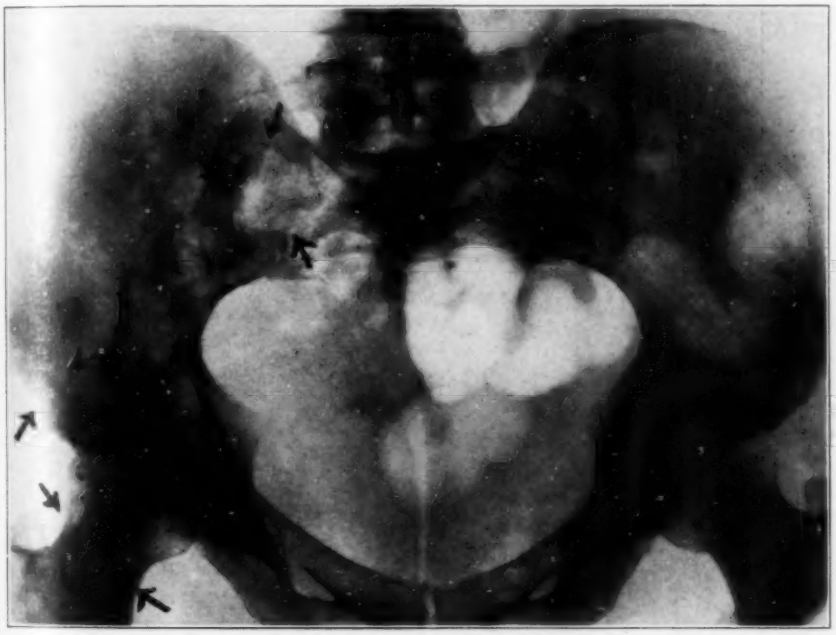

Fig. 4 (case 2).—A metastatic growth involving both wings of the ilium and both femora, especially the right, and the right wing of the sacrum. Unfortunately, a large amount of gas tends to confuse the true areas of metastases, which can be easily differentiated in the original roentgenogram.

requoted from Spiller,[1] there was regionary metastasis, i. e., near the original tumor. This writer reviewed the literature and collected five cases, adding one of his own of multiple gliomatosis of the pia. In three cases there were growths of glial tissue throughout the pia in various parts of the central nervous system.

1. Spiller, W. G.: Gliomatosis of the Pia and Metastasis of Glioma, J. Nerv. & Ment. Dis. **34**:297 (Sept.) 1907.

2. Borst: Die Lehre von den Geschwülsten, vol. 1, quoted by Spiller (footnote 1).

Turner [3] reported a postmortem examination in a case showing a sarcomatous growth in the fourth ventricle of the brain with secondary nodules of growth on the posterior surface of the spinal cord extending to the lumbar region but involving chiefly the cervical portion of the cord. None of the other organs was involved. Powers [4] records a

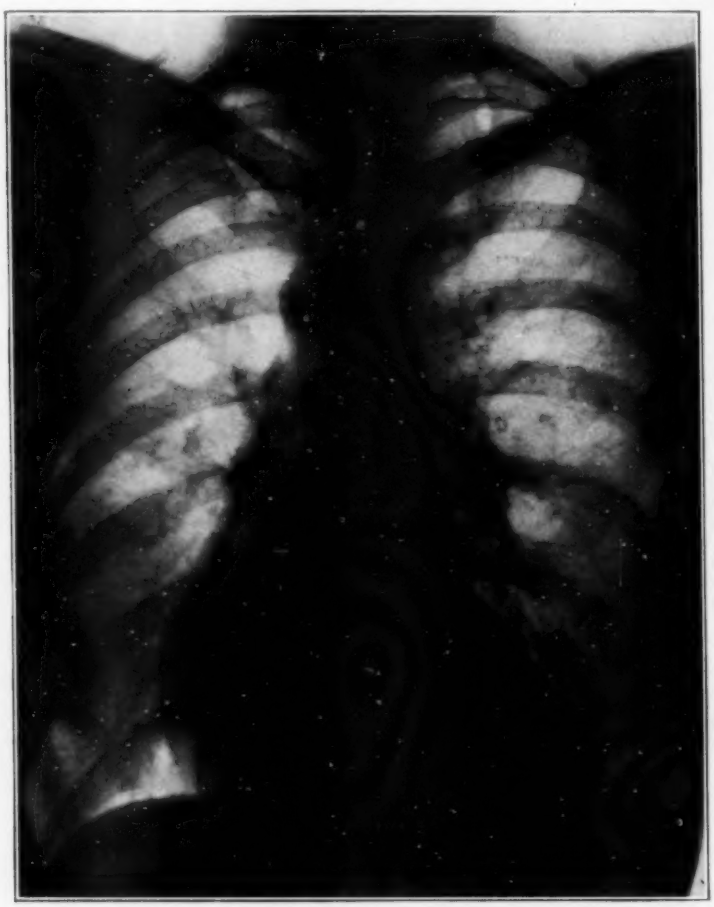

Fig. 5 (case 2).—Lesion in lower part of posterior mediastinum, superimposed by the heart shadow.

case of sarcoma of the left fifth nerve near its origin with multiple sarcomas of the body, but this was a fibrosarcoma and did not actually

3. Turner, G. C.: Sarcomatous Growth in the Fourth Ventricle of the Brain; Secondary Nodules of Growth on the Posterior Surface of the Spinal Cord, Tr. Path. Soc., London **36**:21, 1884-1885.

4. Powers, D'H.: Sarcoma Involving the Left Fifth Nerve Near Its Origin; Multiple Sarcomata of the Body, Tr. Path. Soc., London **37**:65, 1885-1886.

arise in the central nervous system. Perhaps the most interesting case to us from the standpoint of metastasis of tumors of the brain is to be noted in a short article by Turner.[5] He reviewed the postmortem observations in a case demonstrating a gelatinous glioma in the center of the left cerebral hemisphere with a medullary sarcomatous growth in one lung. The latter, which was in the lower part of the upper lobe of the left lung, had been symptomless. It was the size of an orange and caseous. The nearby lymph nodes were not involved, and it was thought to be of independent origin, because the pathologic picture was not like that of the cerebral neoplasm.

Another interesting case reported by Spiller[1] was that of an ependymoma filling the fourth ventricle and extending down to the sixth cervical segment. At the same time there was a small but similar tumor in the lower portion of the thoracic cord, evidently a metastasis.

SUMMARY AND CONCLUSIONS

1. Two cases of tumor of the brain with evidences of a metastatic tumor are reported.

2. These cases are assumed to demonstrate that tumors of the brain metastasize to distant organs because a coincident primary tumor could not be discovered. Postmortem examination was not obtained in either case.

3. We feel justified in presenting these cases, even if they cannot be accepted as evidence that tumors of the brain rarely metastasize to distant organs, for the following reasons: (*a*) The patient in case 1 responded well to irradiation and lived for twelve years after the first treatment. (*b*) In both cases radium was implanted, which demonstrates that such a procedure is safe, if carefully employed. (*c*) Both cases showed evidence of a metastatic tumor, which began either from the tumor or from some other primary lesion that could not be discovered. This fact, in itself, is worthy of note.

4. It seems logical that, if tumors of the brain ever metastasize, we should have a greater opportunity to see and recognize the condition more readily than formerly. The surgical technic and the neurologic and roentgenologic diagnoses are constantly improving, and patients with tumor of the brain should have a greater expectancy of life, thereby increasing the possibility of the development of metastasis.

5. The lesion in each of these cases was a cerebellar tumor. In one case, the tumor was an endothelioma and in the other a glioma (medullary blastoma).

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5. Turner, T. C.: Gelatinous Glioma in the Center of the Left Hemisphere of the Brain with a Medullary Sarcomatous Growth in One Lung, Tr. Path. Soc., London **37**:829, 1885-1886.

CHOLESTEATOMA OF THE BRAIN

REPORT OF A TUMOR OF UNUSUAL SIZE

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Cholesteatomas, although rare, were described as early as 1829 by Cruveilhier,[1] who called them "pearl tumors." Even before this date, LePrestre had probably reported them under the name of tumeur adipociriforme. In 1838, Johannes Müller discovered their laminated structure and named them cholesteatomas. Furthermore, he noted the capsule, saw the polygonal cells without nuclei, called attention to the absence of blood vessels within the tumor and compared them to the horny growths in the skin. Virchow studied them in 1855. He disagreed with Müller in the belief that cholesterin was essential in the tumor and suggested a return to the name of "pearl tumor." Bostroem,[2] in his report in 1897, probably contributed more to the knowledge of these tumors than any one investigator.

ETIOLOGY AND INCIDENCE

Cholesteatomas may be: (1) primary (true tumors) or (2) secondary tumors, which are presumably the result of pre-existing suppuration. The latter condition is also referred to as caseous metamorphosis. Humiston and Piette[3] suggested that the secondary tumor be called inflammatory cholesteatoma, or better still "cholesteatosis."

The secondary type originates as follows: There is a chronic infection or inflammation in the middle ear, the mastoid or in other regions in which this condition is found. In response to this inflammation there is marked proliferation of the epithelium of the mucous membrane, with a later desquamation. This desquamated epithelium cannot be cast off as there is no exit, so it accumulates and undergoes a peculiar degeneration. Politzer gives the usual origin of cholesteatomatous formations in the ear as a pushing in of the epithelium of the external auditory canal through the perforated membrane, and its continuation pathologically so that masses are broken off and tend to pursue independent growth.

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1. Cruveilhier: Anat. path. du corps humaine 1, book 2, plate 6, 1829.

2. Bostroem, E.: Ueber die pialen Epidermoide, Dermoide und Lipome und duralen Dermoide, Centralbl. f. allg. Pathol. u. path. Anat. **8**:1, 1897.

3. Humiston, C. E., and Piette, E. C.: True Cholesteatoma of the Cecum, J. A. M. A. **84**:874 (March 21) 1925.

Wingrave [4] said,

> The normal epithelium of the middle ear is replaced by squamous after prolonged persistence of perforations of the tympanic membrane. The metaplasia is not confined to the tympanum but involves the adjacent pneumatic spaces. The cytolysis and disposal of this rapidly growing new epithelium is difficult, hence it accumulates. Powell White has shown that epithelial metaplasia can be produced by the injection of fatty acids and these acids are constantly present in suppuration of the middle ear.

Virchow considered the presence of cholesteatomatous masses in the temporal bone as a heteroplastic formation. Von Troltsch, Schwartze, Wendt, Lucal, Steinbrugge, Schmiegelow, Uffenorde, Lemaitre and Lavand thought the majority of cholesteatomas were due to metaplasia of the mucous membrane of the middle ear (Lillie and Stark).[5] Erdheim [6] has shown that primary tumors of this type occur in the middle ear, although this was once disputed.

Virchow considered all cholesteatomas due to disturbances of development, and thought that they should be classed as primary. Mikulicz, in 1879, and Kuster, in 1889, were of the same opinion. Bostroem concluded that all cholesteatomas arise from embryonal aberrant epidermal inclusions. He was supported in this view by Beneke [7] and Bonorden. If this be true, the tumors are of congenital origin. Bostroem called this tumor "piale epidermoide," but Bailey [8] said that this is unsatisfactory because these tumors may be extradural and so have no connection with the pia mater. Bailey maintained they are definitely epithelial in origin.

According to Ewing:[9]

> The relation of the medullary groove to the ectoderm, the complex steps in the formation of the brain and ventricles, and the formation and union of the cranial bones give abundant sources for the development of epidermal growths within the skull. The interpretation of these tumors is further complicated by the occasional tendency of endothelial growths to copy the structure of the cholesteatoma, and finally, traumatic implantations of portions of ectoderm account for a small proportion of the intracranial processes.

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4. Wingrave, V. W.: Notes on the Pathogeny of Cholesteatomata, J. Laryngol. Rhinol. & Otol. **25**:339 (July) 1910.

5. Lillie, H. I., and Stark, W. B.: The Insidious, Symptomless Destructive Effect of Cholesteatoma, S. Clin. N Amer. **6**:1359 (Oct.) 1926.

6. Erdheim: Ztschr. f. Ohrenh. **49**:281, 1905.

7. Beneke: Zur Frage der meningealen Cholesteatome, Virchows Arch. f. path. Anat. **142**:429, 1895; Zur Frage der meningealen Cholesteatome, ibid. **149**: 95, 1897.

8. Bailey, P.: Cruveilhier's tumeurs perlées, Surg. Gynec. Obst. **31**:390, 1920. Further Observations on Pearly Tumors, Arch. Surg. **8**:524 (March) 1924.

9. Ewing, J.: Neoplastic Diseases, ed. 2, Philadelphia, W. B. Saunders Company, 1922, p. 974.

An endothelial origin for the deep tumors has been assumed by Glaeser,[10] H. Frank and others. Beneke believed that the meningeal steatomas are produced by a proliferation of endothelial cells of the pia mater. Some pathologists have explained the cholesteatomas as being degenerated endotheliomas, because the tumors in some instances seem to originate in hamartomatous epithelium. Benda[11] held the ependymal epithelium responsible for some deep cholesteatomas. Borst distinguished between intracranial dermoids, epidermoids and endothelial cholesteatomas.

That cholesteatomas of the brain are of rare occurrence is evidenced by the fact that Dana's most recent figures on 100 cases of tumors of the brain give one case of a cholesteatoma. Sachs and Hausman, in a table of 1,658 tumors of the brain compiled by Harvey Cushing, found only eight cholesteatomas and dermoids. Erdheim[6] reported thirteen cholesteatomas at the base of the brain, none of which seemed to be connected with the hypophysis and few were in the midline.

Horrax[12] said that, in a series of 750 verified tumors of the brain from the clinic of Dr. Cushing, there occurred several examples of true intracranial cholesteatomas. In 1920, Bailey[8] reported two of these, of the nonhair-containing variety; another has been reported since, and Horrax added three to the list; these last, however, contained hair, hence they come under the heading of dermoids, or "hair-containing cholesteatomas." Horrax said that the occurrence of cholesteatomas, either hair-containing or otherwise, within the cerebral envelops, from the scalp inward has long been recognized, and that some of these tumors, although not present in the meninges, may still be intracranial, as shown by a recent case reported by Cushing. Horrax further noted that up to 1887 only eighteen reports of the dermoid variety of cholesteatoma could be collected; since then he had found five further cases in an extensive review of the literature, and these, with the three reported by him, make a total of twenty-six cases. In 1920, Bailey reported sixty-two epidermoids, but this relationship to the dermoid variety, Horrax said, is not borne out in the Brigham Hospital series, where, of 750 verified intracranial tumors, three tumors each of the dermoid and epidermoid variety occurred. This makes either type represented by 0.4 per cent of all intracranial tumors. Horrax added that the favorite situations of the dermal and epidermal cholesteatomas are very similar, their most frequent sites being somewhere near the midline at the base of the brain or in the region of the fourth ventricle,

10. Glaeser: Virchows Arch. f. path. Anat. **122**:389, 1890.

11. Benda: Berl. klin. Wchnschr. **37**:1205, 1900.

12. Horrax, Gilbert: A Consideration of the Dermal Versus the Epidermal Cholesteatomas Having Their Attachment in the Cerebral Envelopes, Arch. Neurol. & Psychiat. **8**:265, 1922.

though, in addition, the dermoids have a strong predilection to push into one or the other of the cerebral hemispheres. The one striking point of difference between the dermal and epidermal varieties is that the cerebellopontile angle is one of the most common places for the nonhair-containing tumors, whereas no dermoids have been reported in this location.

In the reports of thirty-two cases of cholesteatoma collected by Bostroem the seat was four times in the fourth ventricle, eight times on the pons and six times on the cerebellum. Boestroem considered the tumor to be of exceedingly slow growth, if congenital, as he thinks.

REPORT OF A CASE

History.—J. T., a white man, single, aged 27, entered Bryce Hospital for the Insane on April 12, 1925. The family history revealed a "peculiar" maternal aunt. He was unable to give a comprehensive history of himself; relatives in writing to the hospital did not furnish much information. The present illness, however, appeared to have begun gradually four or five years previously. The chief complaint was inability to walk straight and unsupported. He also complained of dimness of vision, inability to speak as distinctly as formerly and of vague headache. He did not give any history of convulsions or projectile vomiting.

Physical Examination.—He was fairly well nourished, weighing 126 pounds (57.2 Kg.) and measuring 5 feet, 4½ inches (163.8 cm.) in height. There was no excessive accumulation of subcutaneous fat and the secondary sex characteristics were normal. The tonsils were enlarged and congested. The heart, lungs and abdomen were essentially normal.

Neurologic Examination.—The right eye looked straight forward while the left showed external strabismus. The right eye could follow the finger in a vertical direction only; the left exhibited lateral nystagmus. Vision was practically gone from the right eye, while in the left it was impaired; reading of ordinary print was difficult and the letters appeared blurred. Ophthalmoscopic examination was unsuccessful because of lack of cooperation by the patient. The gait was of the reeling, staggering type, not made worse by closing the eyes. The finger-to-finger test, finger-to-nose test and heel-to-knee test revealed moderate ataxia. The knee jerks were equal and brisk. He was clumsy in efforts to pick up a pin. Adiadokokinesis was present bilaterally. Speech was slow, jerky and stumbling in character. The tongue protruded in the midline, was not atrophied and had no tremor. The positive observations pointed to a cerebellar lesion.

Mental Condition.—The patient was somewhat dull and childish, was not resistive, but did not cooperate well at all times. He had no delusions nor hallucinations.

Laboratory Examination.—The urine had a specific gravity of 1.025, an acid reaction, and the albumin, sugar and the microscopic observations were normal. The blood Wassermann and Kahn tests were negative. The spinal fluid gave a negative Wassermann reaction and a negative globulin test; the cell count was 3 per cubic millimeter and the colloidal gold curve 0000110000.

Course.—Shortly after entering the hospital, he contracted influenza. This was complicated by bronchopneumonia which proved fatal. He did not have convulsions or projectile vomiting while in the hospital.

Necropsy Report.—The subject was slender and fairly well nourished. External examination of the body did not reveal anything of significance.

Within the posterior cranial fossa, was a large, nodular, pearly tumor, situated at the cerebellopontile junction and involving the right cerebral peduncle more than the left.

Within the abdominal cavity, no pathologic lesions of note were observed. The vermiform appendix was large and retrocecal. The spleen was enlarged and grayish, forming the so-called gray acute splenic tumor so common in

Fig. 1.—Base of brain showing pearly tumor in situ.

infections. There were some adhesions around the gallbladder. The thoracic cavity exhibited the lethal lesions. In the left pleural cavity was a sero-sanguineous exudate. There were bilateral apical pleural adhesions. The heart and the pericardium were apparently normal. Both lungs, particularly in the lower lobes, were heavily congested and engorged; they were the seat of confluent bronchopneumonia. Accompanying this pneumonic process was a bilateral purulent bronchitis.

Death was caused by bilateral confluent bronchopneumonia.

Pathologic Anatomy.—The tumor is unique because of its unusual size. Most true cholesteatomas are small and asymptomatic and are accidentally found at necropsy. The total weight of the brain and tumor was 1,215 Gm. The weight of the tumor alone was 69.5 Gm. The dimensions of the tumor were 4 by 5.5 by 8 cm.

The tumor occupied the posterior cranial fossa, distorting, compressing and displacing the nerve tissues. The cerebellum was flattened and exhibited a severe degree of encephalomalacia; the tumor did not invade any tissue. The right hemisphere of the cerebellum was more atrophied by pressure than the left. The pons was likewise flattened as were the cerebral peduncles. The tumor extended anteriorly almost as far as the infundibular stock. The growth was shelled out easily from its bed; it was only loosely attached to the pia mater from which it evidently originated.

Fig. 2.—Base of brain after removal of tumor. Note the compression of cerebellum, pons and peduncles.

The tumor pressed on many of the cranial nerves as they emerged from the brain stem, and this impingement was responsible for the symptoms of dysfunction of the cranial nerve.

The exterior of the tumor had the luster of mother-of-pearl, hence the name "pearly tumor." It was a cystic, spongy mass, composed of multiple nodules, each of which was made up of laminated waxy material. These laminae were undoubtedly layers of flattened cornified squamous cells, somewhat resembling those of the epidermis. The formation of the epithelial layers has been likened to the growth of an onion.

Although the outer surface was white, glistening and pearly, the inner part was yellowish or brownish, resembling sebum, had a caseous feel and possessed a peculiar characteristic odor. The cause of this internal change is a fatty

degeneration. Holinger [13] explained the presence of the cholesterin (which is not an essential ingredient nor a constant observation) by the decomposition of organic matter in an atmosphere in which oxygen is lacking. The degeneration is facilitated and hastened by lack of nutrition. This tumor, in common with others of like nature, had no blood supply and was nourished altogether from the pial vessels and the choroid plexuses. The cholesterin was deposited between the laminations of the squamous epithelium.

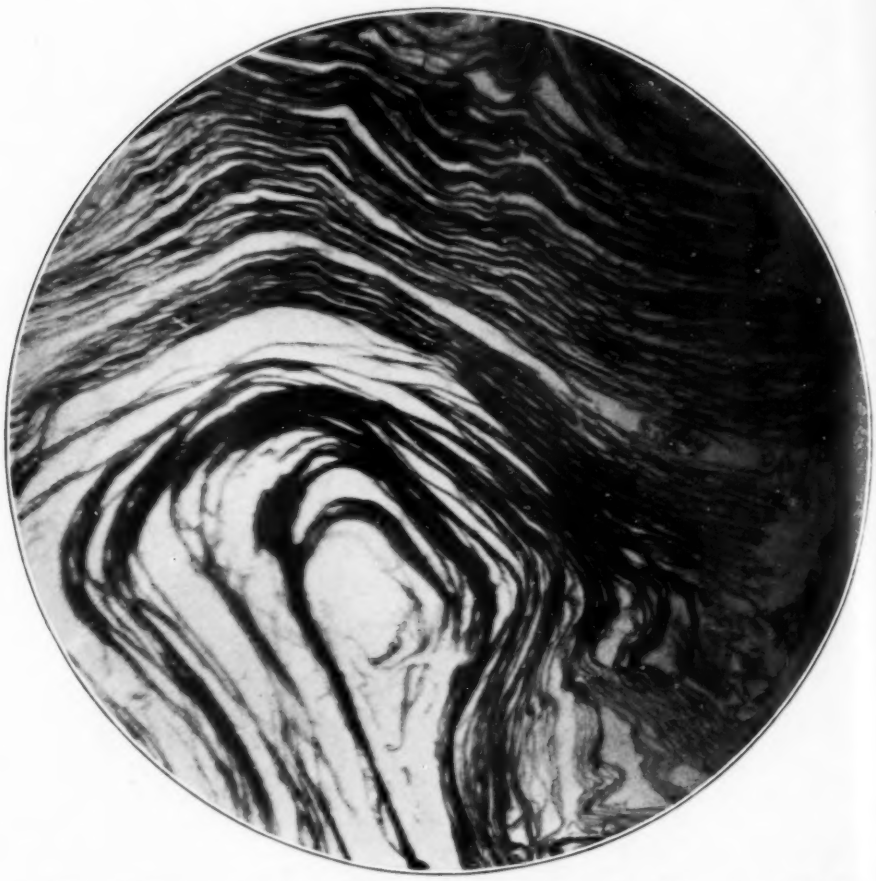

Fig. 3.—Photomicrograph of low power view of cross-section of one of the pearly nodules.

COMMENT

The pearly bodies are nodular and project from the surface of the tumor proper. Bostroem explained this nodule formation by a more rapid growth at a single point, where more cells are thrown off and are arranged concentrically, the increased growth ceasing when the pressure becomes equalized. From the nature of the construction of the

13. Holinger, J.: Varieties of Cholesteatomata, Ann. Otol. Rhin. & Laryng. **10**:254 (May) 1901.

nodules seen microscopically, we feel assured that the cell multiplication is leading to differentiation. In accordance with the observation that tumors made up of cells which are the end-products of tissue differentiation are not malignant, this tumor can be labeled benign. Its manner of growth was expansive rather than infiltrative.

A capsule was lacking over the whole tumor in our case, except at the base or point of attachment to the cerebellum, pons and peduncles, where a heavy partial capsule remained. The tumor seemed to spring from this area, as if it were the fons et origo. Bostroem and later Bailey described this capsular layer as if it were the germinative tissue. They divided it into three layers, which Bailey terms: (1) stratum durum, the connective tissue layer next to the cerebellum; (2) stratum granulosum, composed of nucleated epithelial cells, of which some possess intracellular kerato-hyaline granules and intercellular bridges, the layer as a whole forming the germinative base of the tumor, and (3) the cornified nonnucleated cells which compose the bulk of the tumor growth.

In addition to the base of the brain (intradural and extradural locations), the fourth ventricle and middle ear, cholesteatomatous tumors have been found in the testis, ovary, bone marrow, cecum, antrum of Highmore, urinary passages, gallbladder, mammary gland, uterus, and petrous portion of the temporal bone.

Hair follicles were absent in the tumor reported here; when present they indicate that the tumor is a true dermoid. It is possible for these epithelial growths to become carcinomatous (Ernst).

SUMMARY

A report is given of an unusually large, nonhair-containing, epidermoid cholesteatoma, originating from the pia mater at the cerebellopontile junction.

THE MEASUREMENT OF CEREBRAL AND CEREBELLAR SURFACES

III. PROBLEMS ENCOUNTERED IN MEASURING THE CEREBRAL CORTICAL SURFACE IN MAN *

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INTRODUCTION

In this paper we are concerned with the technical problems bearing on the measurement of the human cerebral cortical surface. This is an anatomic or morphologic method of measuring the capacity of that organ without which we are devoid of the possibility of being intelligent or indeed, of being at all. This method forms a contrast to those which seek to know the capacity of this structure by observing the results of its activity which constitute behavior.

The various aspects of the problem as we now envisage it are as follows: (*a*) the evolution of the main organ of intelligence in various vertebrates from the lowest to man; (*b*) the growth of this organ, i.e., of the surface of the cortex, from fetal life through childhood to the adult; (*c*) the growth of this organ i.e., of the surface of the cortex, from primitive man to modern man; (*d*) variations of the surface in present day man and the differences of race, sex and age; (*e*) variations in the direction of decrease due to disease.

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* From the Neuropathology Laboratory, Montefiore Hospital, New York.

* This work was carried out under the auspices of the Hilda Stich Stroock Fellowship.

* Read before the Fifty-Third Annual Meeting of the American Neurological Association, Atlantic City, N. J., May, 1927.

The division of the brain into functionally different cytoarchitectonic areas should be the next step in this large and difficult undertaking.

HISTORICAL SUMMARY

R. Wagner,[1] in 1862, was the first to study the extent of the cortical surface of the human brain. In 1864, H. Wagner [2] carried on the work his father had begun. He covered the cortical surface of the brain with thin gold leaf. The length and depth of the fissures were measured directly. The brain was preserved in alcohol. He found the surface to be 221,005 sq. mm. In 1875, Jensen [3] employed the same method except that he used tinfoil in 5 mm. squares instead of gold leaf. The length and depth of the fissures were measured in a way similar to that used by Wagner. The surface within the fissures was not accurately determined.

In 1901, Anton [4] cut series of frontal sections of the cerebrum and measured the gray and white matter by means of a planimeter. From these he computed the total surface area; his results were similar to those obtained by Wagner. Yager [5] used the same method as Anton and found about the same results. Baillarger,[6] who dissected, unfolded and measured the whole extent of the cortex, found an area of 170,000 sq. mm. Paulier [7] used the same method as Wagner and obtained a result similar to that of Baillarger.

Calori [8] measured forty-one brains and found the following results for the total surface: male, brachycephalic, 247,773 sq. mm.; male, dolichocephalic, 230,212; female, brachycephalic, 211,701; female, dolichocephalic, 198,210.

Danilewsky [9] attempted to determine the area of the whole cortex by a comparison of the weight of the brain, the specific gravity, the specific gravity of the gray matter, the specific gravity of the white matter and the average thickness of the gray matter. By this method

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1 Wagner, R.: Vorstudien einer wissenschaftlichen Morphologie und Physiologie des menschlichen Gehirns als Seelenorgan, 1862.

2. Wagner, H.: Massbestimmung der Hirnoberflache, Göttingen, 1864.

3. Jensen: Untersuchungen über die Beziehungen zwischen Grosshirn und Geistesstorung, Arch. f. Psychol., 1875, vol. 5.

4. Anton: Gehirnvermessung mittels des Kompensations Polar Planimeter, Wien. klin. Wchnschr. **46**:1263, 1903.

5. Yager: Inhaltsberechnung der Rindensubstanz, Arch. f. Psychiat. **54**:261, 1914.

6. Cited in Tilney and Riley: Forms and Functions of the Central Nervous System, New York, Paul B. Hoeber, 1921, p. 757.

7. Paulier: Récherches sur la notion de surface en anatomie, determination de la surface du cerveau, Paris, 1892.

8. Cited in Quain's Anatomy, 1909, vol. 3, part 1, p. 341.

9. Cited in Quain's Anatomy, vol. 3, pt. 1, p. 341.

he obtained the total surface 169,200 sq. mm.. for the average brain. Donaldson [10] calculated the human cortical surface and found the relation of the exposed area to the sunken area to be 1 : 2, i.e., a relation of the visible to the total surface, 1 : 3. The total surface area found was 200,000 sq. mm.

Henneberg [11] undertook the measurement of the surface of the human cortex in 1910. He hardened the brains in a solution of formaldehyde, cut sections 1 cm. square along the fissures and sulci, covered these with millimeter paper and measured their surface. He measured three brains of Europeans and one each of a Hottentot, a Herero and a Javan. He made further studies in cases of dementia paralytica and senile dementia. He confirmed the results of Wagner and estimated the total surface of the cortex to be 226,200 sq. mm., the visible surface, 77,000 sq. mm. and the relation of visible to total surface 1 : 2.94. He found that the surface of the left hemisphere was greater than the right and vice versa in an equal number of cases. In his studies of the Hottentot and Javan brains, he found a surface area equal to those of the Europeans. The Herero brain had a smaller surface. The cortices of the brains of persons having dementia paralytica and senile dementia showed a smaller surface area.

In 1926, Ditto and one of us (W. M. K.) [12] devised another method. This paper gives an account of the problems and technic of the application of this method.

TECHNIC OF PREPARATION

Removal, Weighing and Estimation of the Volume of the Fresh Brain.—After removal of the brain from the skull and removal of the dura, the brain is weighed. The brain should not be used when the person has been dead longer than twenty-four hours. The volume of the brain is determined by displacement in a glass vessel containing a measured amount of water.

A small incision is made along the sagittal sulcus through the corpus callosum to allow the water to penetrate into the ventricles.

Weighing and Estimation of Volume of the Brain in the Different Fixing Agents.—Solution of Formaldehyde: The brain is placed in 4 liters of 10 per cent liquor formaldehydi (1 liter of 40 per cent formaldehyde and 3 liters of water) It is left in this fixative for three weeks. At the end of three weeks, it is weighed and its volume is determined by displacement, 10 per cent liquor formaldehydi being used instead of water.

Water: The brain is then put into running water for twenty-four hours.

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10. Donaldson, H. H.: Anatomical Observations on the Brain and Several Sense Organs of the Blind Deaf Mute, Am. J. Psychol. **3**:293, 1890-1891.

11. Henneberg: Messung der Oberflachenausdehung der Grosshirnrinde, J. f. Psychiat. u. Neurol. **17**:145, 1910.

12. Kraus, W. M., and Ditto, M. W.: A Method of Measuring the Cerebral and Cerebellar Cortical Surfaces, Arch. Neurol. & Psychiat. **17**:193 (Feb.) 1927.

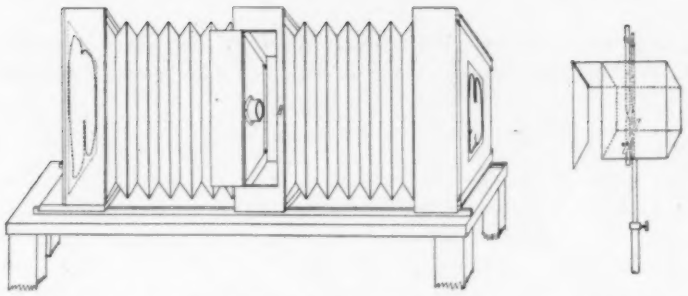

Fig. 1.—On the right is a strong carbon light. An opaque shield is hung in front of the light. The bellows have a maximum length of 6 feet, a height of 18 inches and a width of 12 inches. The slide is placed in a plate holder on the right. The image passes through the lens in the middle frame and, enlarged, is projected on a ground glass on the left. The lens holding the frame can be moved to adjust the focus. The image is traced on transparent paper attached to the ground glass.

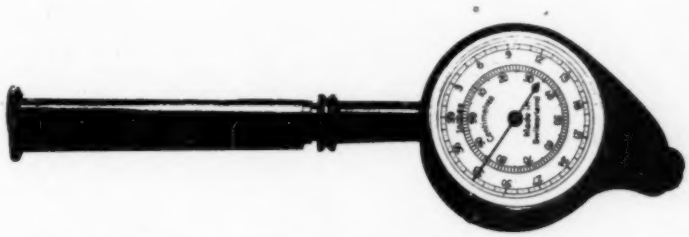

Fig. 2.—The curvometer or rotary map measuring device.

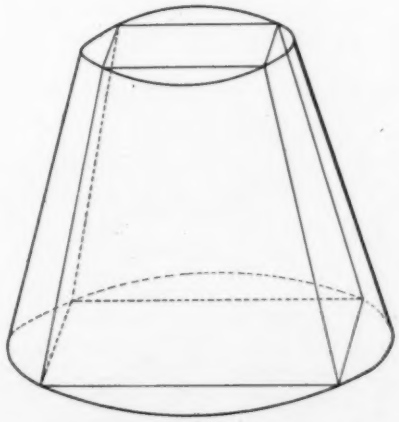

Fig. 3.—Geometric figure to illustrate the transformation of the surface between two sections into the frusta of a truncated pyramid and a truncated cone.

Alcohol: (*a*) The brain is immersed in 80 per cent alcohol for forty-eight hours, three times the original volume of the brain being used. After forty-eight hours, the weight and volume are determined as before except that the volume is determined in 80 per cent alcohol.

(*b*) The brain is immersed in 95 per cent alcohol for from forty-eight to seventy-two hours, three times the original volume being used. At the end of this period, the weight and volume are determined as before except that the volume is determined in 95 per cent alcohol.

(*c*) The brain is transferred into absolute alcohol for forty-eight hours, three times its original volume being used. Weight and volume are determined as before, except that the volume is determined in absolute alcohol.

(*d*) The brain is transferred into absolute alcohol and ether, equal parts, for twenty-four hours, twice the original volume being used. Weight and volume are determined as before, except that the volume is determined in absolute alcohol and ether.

Embedding.—The brain is embedded in 3 per cent parlodion for three days. The parlodion should cover the whole brain. The specimen is embedded in a known volume of 6 per cent parlodion by slow evaporation (from six to eleven weeks). The weight and volume are calculated after hardening is completed.

Mounting and Cutting.—The block is mounted and cut in 80 per cent alcohol by a Sartorius microtome. The sections are cut at 100 microns and are cut continuously to prevent shrinkage.

Staining and Mounting.—The specimen is stained by the method of Loyez and mounted in balsam.

Projection and Drawing.—The slide is projected and enlarged by means of a photographic camera (fig. 1). The lens used is a 120 mm. Leitz microsummar lens. A 5 cm. line is drawn on the slide, and this is projected on the enlarged drawing, thus establishing the enlargement.

The drawing is made from the projection, India ink being used. When this is done, reference is always made to the section to see whether any errors were made in the drawing. A microscope lens is used to correct the errors.

Measuring.—The perimeters of each hemisphere are measured with the rotary map measuring device or curvometer (fig. 2), and the measurements are reduced to normal values. The height is already known, 100 microns or 0.1 mm.

CALCULATION AND FORMULAS

As the cerebral hemispheres have a somewhat elliptic form, the formula of a truncated cone is best suited for the calculation of its surface. In figure 3 a truncated cone is superimposed on a truncated pyramid. The lateral surfaces are the frusta. The formula for the area of the frustum of a truncated cone is

$$s \times \frac{A + B}{2}$$

s is the slant line corresponding to the height; $\frac{A + B}{2}$ are the circumferences of the outlines of sections taken at given intervals.

The formula for the determination of shrinkage of surface will be given by one of us (A. W.) in another paper. We have kept records of the gain and loss in weight and volume of several embryo and adult

brains as they passed through the different fixing agents. Table 1 shows the loss in weight, volume and surface area of one embryo and two adult brains. This table shows that the embryo brain lost 70.5 per cent in weight, 69 per cent in volume and 54 per cent in surface area. Considering that the fetal brain contains a large amount of water, this loss is not at all surprising.

When the tables showing the amount of shrinkage and the curve of the adult brains are examined, it is seen that there is a loss of from 27 to 29 per cent in weight, of from 12 to 13 per cent in volume, and of from 8 to 9 per cent in surface (table 1 and fig. 4).

TABLE 1.—*Determination of Loss of Surface Area of Cerebrum Due to Shrinkage*

	Weight			Volume			Surface Calculated as the Surface of a Globe		
	Gm.	Per Cent	Per Cent Loss	Cc.	Per Cent	Per Cent Loss	Sq.cm.	Per Cent	Per Cent Loss
Embryo Brain, 4 Months									
Original weight	50.00	100.00	.....	50.00	100.00	.....	65.60	100.00	.....
Solution of formaldehyde	50.00	100.00	.....	50.00	100.00	.....	65.60	100.00	.....
Alcohol, 80 per cent	25.50	51.00	49.00	24.00	48.00	52.00	46.60	71.00	29.00
Alcohol, 95 per cent	16.30	33.00	67.00	16.50	33.00	67.00	32.20	49.00	51.00
Absolute alcohol	14.80	29.60	70.40	15.80	31.00	69.00	30.50	46.50	53.50
Absolute alcohol and ether	14.70	29.50	70.50	15.70	31.00	69.00	30.30	46.00	54.00
Adult Brain, 42 Years									
Original weight	1500.00	100.00	.....	1475.00	100.00	.....	627.00	100.00	.....
Solution of formaldehyde	1510.00	100.6	.....	1525.00	103.00	.....	641.00	102.00	.....
Alcohol, 80 per cent	1455.00	96.00	4.00	1450.00	99.00	1.00	624.00	99.50	0.50
Alcohol, 95 per cent	1250.00	83.00	17.00	1320.00	89.00	11.00	584.00	93.00	7.00
Absolute alcohol	1170.00	78.00	22.00	1300.00	88.00	12.00	576.00	92.00	8.00
Absolute alcohol and ether	1090.00	73.00	27.00	1300.00	88.00	12.00	576.00	92.00	8.00
Adult Brain, 36 Years									
Original weight	1480.00	100.00	.....	1435.00	100.00	0	615.00	100.00	.....
Solution of formaldehyde	1560.00	105.50	.....	1550.00	108.00	.....	648.00	105.00	.....
Alcohol, 80 per cent	1482.00	100.00	.....	1510.00	105.00	.....	636.00	103.00	.....
Alcohol, 95 per cent	1302.00	88.00	12.00	1370.00	95.50	4.50	601.00	98.00	2.00
Absolute alcohol	1140.00	77.00	27.00	1300.00	91.00	9.00	576.00	94.00	6.00
Absolute alcohol and ether	1050.00	71.00	29.00	1250.00	87.00	13.00	561.00	91.00	9.00

From the foregoing tables it is evident that the brains gain in weight after they are placed in solution of formaldehyde. When the brain passes through the different dehydrants, there is a loss of 9 per cent in surface, if we consider the brain as a globe.

Calculation in Forty-one Consecutive Sections.—The next problem was to ascertain the greatest interval between successive sections which would permit accurate measurement of the cerebral cortex. In other words, would it be necessary to measure every section, every second or every third section, etc.? To obtain this information, we measured and calculated the surface for forty-one consecutive sections. The total visible surface (without the median longitudinal fissure) was measured. Tables 2, 3 and 4 give the data.

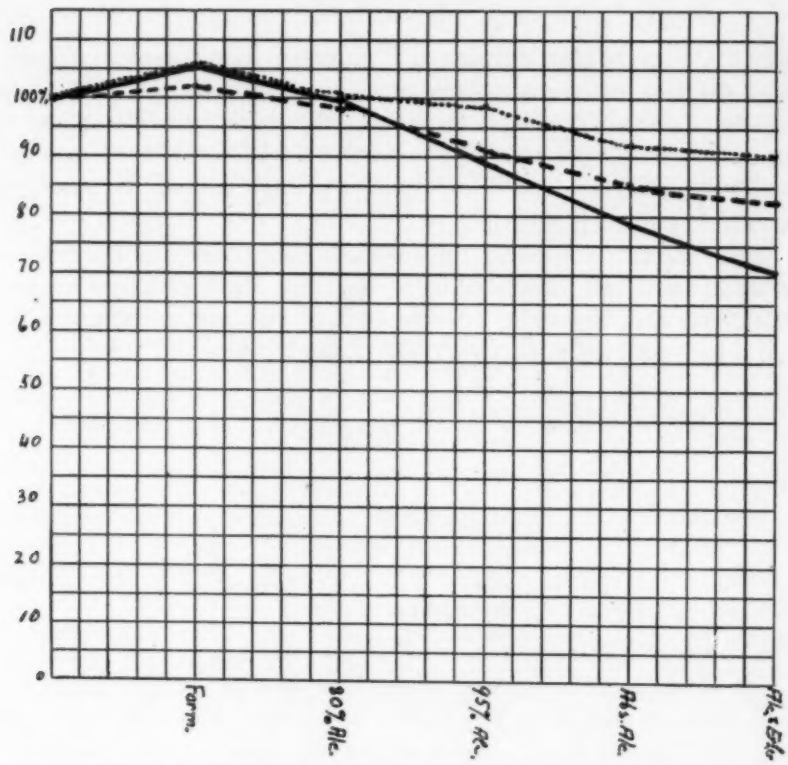

Fig. 4.—Graph showing the loss in weight, volume and surface during the different processes of embedding the brain. The solid line indicates weight; the broken line, volume, and the dotted line, surface.

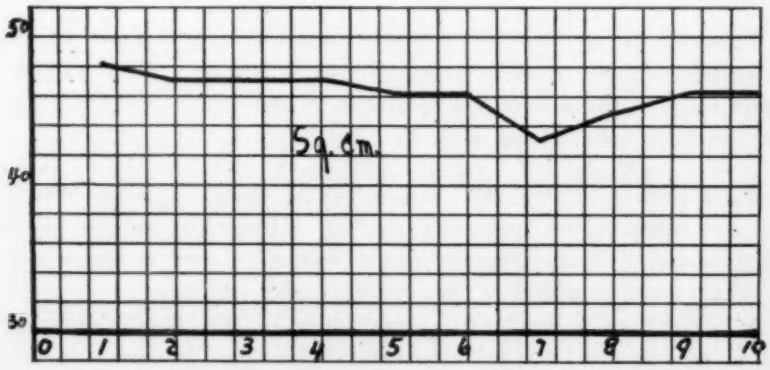

Fig. 5.—Graph showing visible surface of cerebrum of forty-one consecutive sections taken at different intervals.

TABLE 2.—*Perimeters for Calculating the Visible Surface Area of Cerebrum in Forty-One Consecutive Sections*

Right Visible Perimeter		Left Visible Perimeter	
Section Number	Perimeter, Cm.	Section Number	Perimeter, Cm.
352	16.00	352	18.85
353	16.00	353	18.90
354	16.10	354	18.90
355	16.20	355	19.00
356	16.40	356	19.10
357	16.50	357	19.20
358	16.60	358	19.40
359	16.80	359	19.40
360	16.90	360	19.50
361	17.00	361	19.70
362	17.00	362	19.90
363	17.10	363	20.00
364	17.40	364	20.10
365	17.60	365	20.40
366	17.80	366	20.50
367	17.90	367	20.60
368	17.90	368	20.80
369	18.00	369	21.00
370	18.10	370	21.00
371	18.20	371	21.10
372	18.30	372	21.30
373	18.30	373	21.20
374	18.30	374	21.30
375	18.40	375	21.50
376	18.30	376	21.60
377	18.20	377	21.80
378	18.20	378	21.90
379	18.10	379	21.90
380	18.20	380	22.00
381	18.20	381	22.00
382	18.10	382	22.10
383	18.30	383	21.90
384	18.20	384	21.80
385	18.40	385	21.60
386	18.20	386	21.30
387	18.10	387	21.20
388	18.20	388	21.00
389	18.10	389	20.80
390	18.10	390	20.70
391	18.10	391	20.50
392	18.00	392	20.50
41 sections =	716.80	41 sections =	868.35
Average =	17.48	Average =	21.18

TABLE 3.—*Visible Surface Area of Cerebrum in Forty-One Consecutive Sections (Calculated as the Sum of the Frusta of Truncated Cones)*

Section Number	Perimeter (Cm.)	Radius (Cm.)	$r-r_1$ (Cm.)	$\frac{A+B}{2}$ (Cm.)	s (Cm.)	S (Sq.Cm.)
352	34.85	5.550	0.000	34.85	0.0100	0.3485
353	34.90	5.558	0.008	34.87	0.0125	0.4357
354	35.00	5.570	0.012	34.95	0.0155	0.5415
355	35.20	5.610	0.040	35.10	0.0410	1.4440
356	35.50	5.658	0.048	35.35	0.0490	1.7310
357	35.70	5.680	0.040	35.60	0.0410	1.4600
358	36.00	5.740	0.060	35.85	0.0605	2.1690
359	36.30	5.780	0.040	36.15	0.0410	1.4830
360	36.60	5.820	0.040	36.45	0.0410	1.4995
361	36.90	5.860	0.040	36.75	0.0410	1.5090
362	37.00	5.880	0.020	36.95	0.0225	1.8230
363	37.20	5.915	0.035	37.10	0.0365	1.3550
364	37.40	5.950	0.035	37.30	0.0365	1.3610
365	37.70	6.000	0.050	37.55	0.0510	1.9150
366	38.30	6.095	0.045	38.00	0.0450	1.7100
367	38.40	6.110	0.015	38.35	0.0180	0.6405
368	38.70	6.160	0.050	38.55	0.0510	1.9650
369	39.00	6.205	0.045	38.85	0.0460	1.7900
370	39.10	6.215	0.010	39.05	0.0145	0.5655
371	39.30	6.255	0.040	39.20	0.0410	1.6060
372	39.60	6.305	0.050	39.45	0.0510	2.0100

TABLE 3.—*Visible Surface Area of Cerebrum in Forty-One Consecutive Sections (Calculated as the Sum of the Frusta of Truncated Cones)—Continued*

Section Number	Perimeter (Cm.)	Radius (Cm.)	$r-r_1$ (Cm.)	$\frac{A+B}{2}$ (Cm.)	s (Cm.)	S (Sq.Cm.)
373	39.50	6.290	0.015	39.55	0.0180	0.7120
374	39.60	6.305	0.015	39.55	0.0180	0.7120
375	39.90	6.355	0.050	39.75	0.0510	2.0300
376	39.90	6.355	0.000	39.90	0.0100	0.3990
377	40.00	6.370	0.015	39.95	0.0180	0.7200
378	40.10	6.385	0.015	40.05	0.0180	0.7250
379	40.00	6.370	0.015	40.05	0.0180	0.7250
380	40.20	6.400	0.030	40.10	0.0315	1.2630
381	40.20	6.400	0.000	40.20	0.0100	0.4200
382	40.20	6.400	0.000	40.20	0.0100	0.4200
383	40.20	6.400	0.000	40.20	0.0100	0.4200
384	40.00	6.370	0.030	40.10	0.0315	1.2630
385	40.00	6.370	0.030	40.00	0.0315	1.2600
386	39.50	6.290	0.020	39.75	0.0225	0.8950
387	39.30	6.255	0.045	39.45	0.0460	1.8390
388	39.20	6.240	0.015	39.25	0.0180	0.7080
389	38.80	6.175	0.065	39.00	0.0660	2.5750
390	38.80	6.175	0.000	38.80	0.0100	0.3880
391	38.60	6.145	0.030	38.70	0.0315	1.2200
392	38.50	6.130	0.015	38.55	0.0180	0.6950
			Total =	1569.42		48.71 sq.cm.
			Average $\frac{A+B}{2}$ =	38.27		

TABLE 4.—*Visible and Total Surface Area of Cerebrum in Forty-One Consecutive Sections*

Section Number	Perimeter for Visible Surface (Cm.)	Perimeter for Total Surface (Cm.)	Ratio	S Visible Surface (Sq.Cm.)	S Total Surface (Sq.Cm.)
352	34.85	174.00	4.96	0.3485	1.730
353	34.90	174.00	4.98	0.4357	2.168
354	35.00	175.00	5.00	0.5415	2.709
355	35.20	174.50	4.95	1.4440	7.130
356	35.50	172.50	4.86	1.7310	8.450
357	35.70	175.50	4.91	1.4600	7.170
258	36.00	177.50	4.92	2.1690	10.700
359	36.30	179.00	4.93	1.4830	7.300
360	36.60	181.00	4.94	1.4995	7.400
361	36.90	177.50	4.81	1.5090	7.400
362	37.00	178.50	4.82	1.8230	8.970
363	37.20	179.50	4.82	1.3550	6.635
364	37.40	180.50	4.82	1.3610	6.700
365	37.70	181.50	4.81	1.9150	9.410
366	38.30	182.50	4.76	1.7100	8.320
367	38.40	181.50	4.72	0.6405	3.210
368	38.70	183.50	4.74	1.9650	9.520
369	39.00	186.00	4.76	1.7900	8.700
370	39.10	186.50	4.77	0.5665	2.758
371	39.30	184.50	4.70	1.6090	7.730
372	39.60	187.50	4.74	2.0100	9.700
373	39.50	191.00	4.83	0.7120	3.440
374	39.60	193.00	4.87	0.7120	3.465
375	39.90	194.50	4.87	2.0300	9.900
376	39.90	194.00	4.86	0.3990	1.940
377	40.00	194.00	4.85	0.7200	3.492
378	40.10	193.00	4.81	0.7250	3.492
379	40.00	191.00	4.76	0.7250	3.458
380	40.20	191.00	4.74	1.2630	5.990
381	40.20	190.00	4.72	0.4200	1.982
382	40.20	192.00	4.77	0.4200	2.005
383	40.20	194.50	4.83	0.4200	2.030
384	40.00	193.00	4.82	1.2630	6.100
385	40.00	194.50	4.86	1.2600	6.140
386	39.50	194.50	4.87	0.8950	4.358
387	39.30	197.00	5.01	1.8390	9.180
388	39.20	197.00	5.02	0.7080	3.537
389	38.80	196.00	5.05	2.5750	12.850
390	38.80	195.00	5.02	0.3880	1.937
391	38.60	197.50	5.12	1.2200	6.110
392	28.50	198.00	5.14	0.6950	3.490
Total			....	48.71	238.24
Average ratio			4.85		

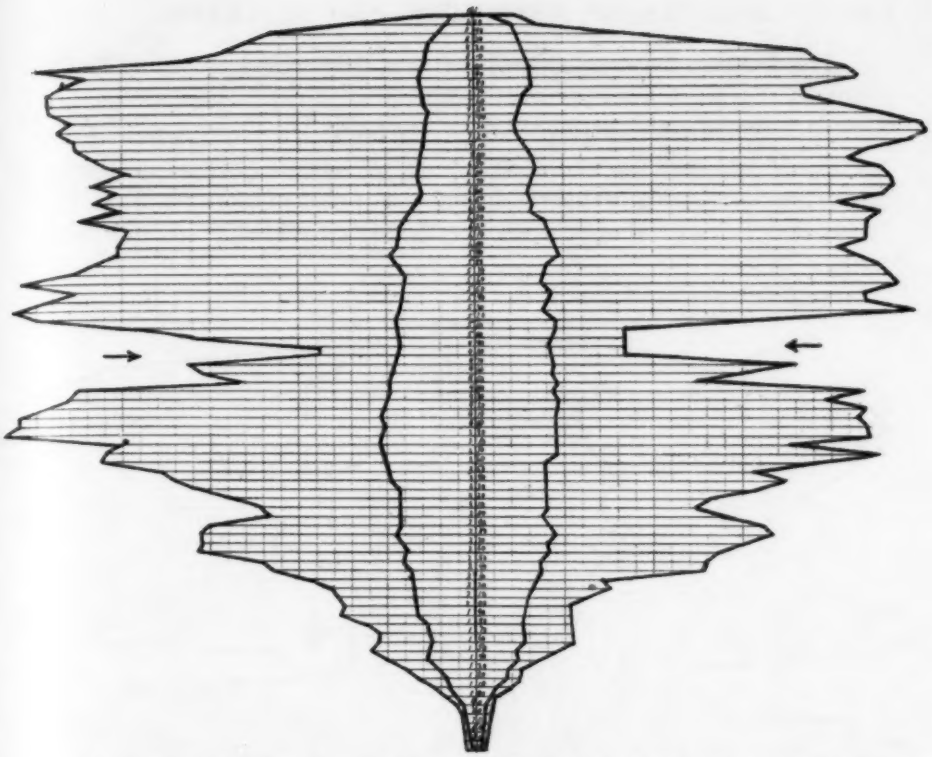

Fig. 6.—Graphic representation of the perimeters of the visible surface, without the median longitudinal fissure, plus the total surface of each cortical section. The small area in the center is the visible surface. The ratio of the visible to the total surface in this case is about 4.50 : 1. The arrows in the center of the section indicate the great variations in the perimeters. This is due to the cutting of the brain into two halves. The gaps in the different areas are due to the natural variations of the sections as explained in the text.

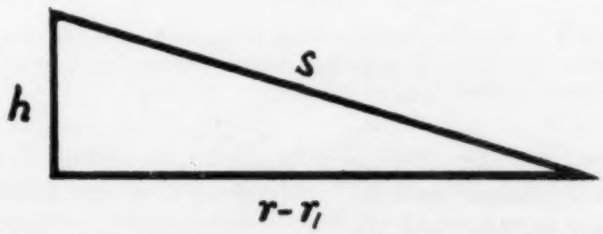

Fig. 7.—Diagram to illustrate the calculation of the slant height graphically, r-r_1, is the difference of the radii of the perimeters of the upper and lower section transformed into circles; h is the distance between two sections and s is the slant height.

The frustum between each section was determined according to the formula of a frustum of a truncated cone $\left(s \times \frac{A+B}{2}\right)$. The slant line ($s$) can also be determined graphically by laying down $r\text{-}r_1$ (radius of the perimeter transformed into a circle) and h (the height) on millimeter paper, and enlarging 100 times in order to avoid errors (fig. 7). The slant line (s) can be measured directly by a finely divided millimeter ruler.

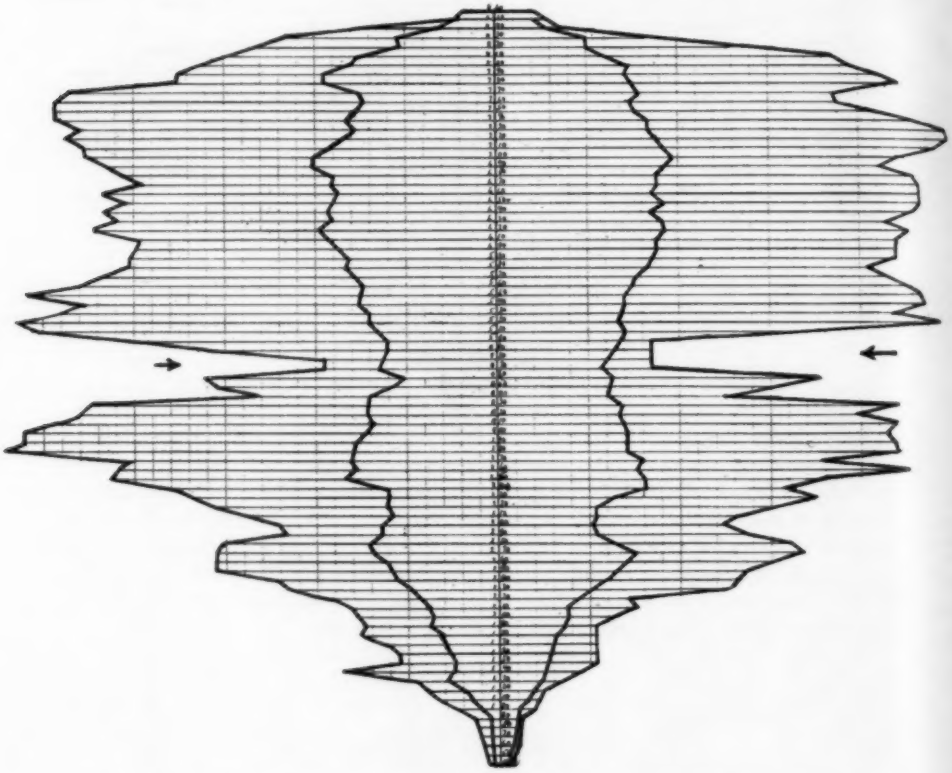

Fig. 8.—A representation similar to that in figure 6. In this case the visible surface includes the median longitudinal fissure, giving a ratio of the visible to the total surface of about 3:1.

Each slant line (s) is multiplied by $\frac{A+B}{2}$, the average of the perimeters of two adjacent sections. This gives S or the lateral surface between these sections (table 3).

All of the $\frac{(A+B)'s}{2}$ are added and then divided by the number of sections measured. The result is the average perimeter. For the forty-one consecutive sections, this was 38.27 cm. (table 3).

TABLE 5.—*Perimeters for Calculating Total Surface Area of Cerebrum in Forty-One Consecutive Sections*

Right		Left	
Section	Perimeter (Cm.)	Section	Perimeter (Cm.)
352	86.50	352	87.50
353	86.50	353	87.50
354	87.00	354	88.00
355	85.00	355	89.50
356	82.00	356	90.50
357	82.00	357	93.50
358	82.00	358	95.50
359	81.50	359	97.50
360	83.50	360	97.50
361	82.50	361	95.00
362	82.50	362	96.00
363	83.00	363	96.50
364	84.00	364	96.50
365	84.50	365	97.00
366	85.00	366	97.50
367	84.00	367	97.50
368	85.00	368	98.50
369	86.50	369	99.50
370	87.00	370	99.50
371	85.50	371	99.00
372	87.50	372	100.00
373	90.50	373	100.50
374	92.00	374	101.00
375	93.00	375	101.50
376	93.00	376	101.00
377	93.00	377	101.00
378	92.00	378	101.00
379	90.00	379	101.00
380	90.00	380	101.00
381	88.50	381	101.50
382	90.00	382	102.00
383	92.00	383	102.50
384	91.50	384	101.50
385	92.00	385	102.50
386	91.50	386	103.00
387	93.00	387	104.00
388	93.50	388	103.50
389	92.50	389	103.50
390	91.00	390	104.00
391	93.00	391	104.50
392	93.50	392	104.50
41 sections =	3608.50	41 sections =	4044.50
Average =	88.01	Average =	98.64

TABLE 6.—*Surface Area of Cerebrum in Forty-One Consecutive Sections*

	Hemisphere	Surface Without Shrinkage (Sq.Cm.)	Surface With Shrinkage of 9 per Cent (Sq.Cm.)	Average $\frac{A+B}{2}$ (Cm.)	Ratio of the Perimeters for Visible and Total Surfaces
Visible surface area	Right	22.04	24.03	17.48	5.03 : 1
	Left	26.66	29.05	21.18	4.65 : 1
	Both	48.70	53.08	38.66	4.84 : 1
Total surface area	Right	110.86	120.87	88.01	1 : 5.03
	Left	123.96	136.11	98.64	1 : 4.65
	Both	234.82	256.98	186.65	1 : 4.84

The $\frac{(A+B)'s}{2}$ of the right and left visible hemispheres were added separately; the average perimeter for the right hemisphere was 17.48 cm. and the average perimeter for the left hemisphere was 21.18 cm. (table 2). The average for both the right and the left hemispheres was

38.66 cm., which approximates 38.27, the average perimeter of the total visible surface of both hemispheres.

The average $\frac{(A+B)'s}{2}$ for the total surface of the right and left hemispheres were found (table 5). The average perimeter for the total right hemisphere was 88.01 cm. and for the total left hemisphere, 98.64 cm. (table 5). The average perimeter for both right and left hemispheres was 186.65 cm. (table 6).

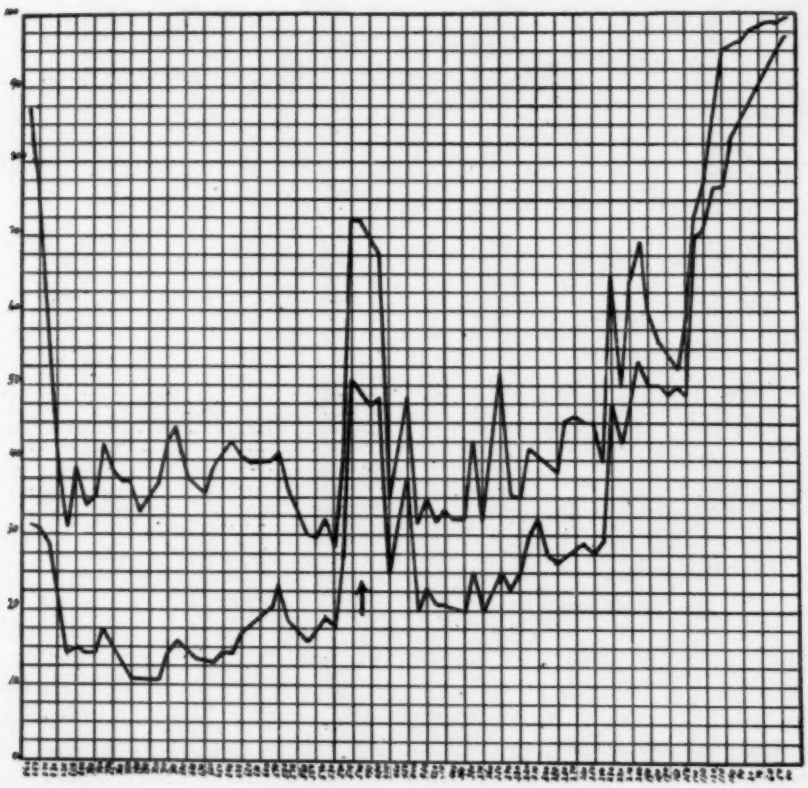

Fig. 9.—A combination of figures 6 and 8 showing the percentage relation of the visible surfaces. The upper curve is the percentage relation of the visible surface, with the median longitudinal fissure, to the total surface. The lower curve is the percentage relation of the visible surface, without the median longitudinal fissure, to the total surface. The abscissa indicates the horizontal sections of the brain. The ordinates indicate percentages of the perimeters of visible to total surfaces, which is 100 per cent.

The relation of the perimeters of the total and visible surfaces is found by dividing

$$\frac{\text{Total Perimeter}}{\text{Visible Perimeter}} = \frac{186.65}{38.66} = 4.84 \text{ (tables 4 and 6).}$$

The same can be done for each section separately (table 4). For the right hemisphere the perimeters have a ratio of 5.03 : 1 and for the left hemisphere, 4.65 : 1. The average of these two ratios is 4.84. The total surface is obtained by multiplying the visible surface by the ratio of the visible to the total surface perimeters.

The visible surface for the forty-one consecutive sections determined according to the formula of a truncated cone is 48.71 sq. cm. (tables 3 and 6). By multiplying 48.71 sq. cm. by 4.84, we find the total surface of the forty-one sections to be 234.82 sq. cm. The right total surface is 110.86 sq. cm.; the left, 123.96 sq. cm. By adding to this 9 per cent, due to shrinkage, we find the total surface of the forty-one sections in

Figure 10

Figure 11

Fig. 10.—Contour of horizontal section of the cerebrum taken at the vertex (section 860).

Fig. 11.—Contour of horizontal section of the cerebrum following figure 10 (section 840), showing the differences in size and the appearance of new fissures.

both hemispheres to be 256.98 sq. cm., the right being 120.87 sq. cm., and the left, 136.11 sq. cm. (table 6).

In order to determine the interval of sections needed for accuracy, we calculated by this method the surface between every second, third, fourth, fifth, sixth, seventh, eighth, ninth and tenth sections (table 7 and fig. 5). These tables and curves show that for the human cerebral cortex every tenth section suffices for accurate measurements and calculations.

TABLE 7.—*Visible Surface Area of Cerebrum in Forty-One Consecutive Sections, Showing that Measuring Only Every Tenth Section Does Not Introduce Any Error of Importance*

	Sq. Cm.
Every section	48.72
Every second section	47.18
Every third section	47.60
Every fourth section	48.54
Every fifth section	46.09
Every sixth section	46.60
Every seventh section	43.36
Every eighth section	47.83
Every ninth section	46.31
Every tenth section	46.65

Visible Surface Areas of Cerebrum in Forty-One Sections to Determine the Interval Between Sections at Which an Appreciable Error Will Occur

Section Number	Perimeter (Cm.)	r (Cm.)	$r-r_1$ (Cm.)	$\frac{A+B}{2}$ (Cm.)	s (Cm.)	$s \times \frac{A+B}{2}$ (Sq. Cm.)
			A. Every Second Section			
352	34.90	5.55	0.00	34.90	0.0200	0.698
354	35.20	5.60	0.05	35.05	0.0640	1.892
356	35.70	5.70	0.10	35.45	0.1020	3.620
358	36.30	5.80	0.10	36.00	0.1020	3.710
360	36.90	5.88	0.08	36.60	0.0830	3.040
362	37.20	5.93	0.05	37.05	0.0540	2.050
364	37.70	6.01	0.08	37.45	0.0830	3.100
366	38.40	6.12	0.11	38.05	0.1100	4.260
368	38.70	6.16	0.04	38.55	0.0445	1.710
370	39.30	6.26	0.10	39.00	0.1020	3.980
372	39.50	6.29	0.03	39.40	0.0360	1.420
374	39.90	6.36	0.05	39.70	0.0540	2.140
376	40.00	6.38	0.04	39.95	0.0445	1.780
378	40.00	6.38	0.00	40.00	0.0200	0.800
380	40.20	6.41	0.03	40.10	0.0360	1.450
382	40.20	6.41	0.00	40.20	0.0200	0.802
384	40.20	6.38	0.03	40.10	0.0360	1.430
386	39.30	6.30	0.08	39.65	0.0830	3.295
388	38.80	6.18	0.12	39.05	0.1210	3.990
390	38.60	6.15	0.03	38.70	0.0360	1.390
392	38.60	6.15	0.00	38.60	0.0200	0.626
					Total =	47.18 sq. cm.
			B. Every Third Section			
352	34.90	5.55	0.00	34.90	0.3000	1.050
355	35.50	5.66	0.11	35.20	0.1140	4.020
358	36.30	5.80	0.14	35.90	0.1430	5.150
361	37.00	5.90	0.10	36.65	0.1040	3.810
364	37.70	6.01	0.11	37.35	0.1140	4.250
367	38.70	6.16	0.15	38.20	0.1525	5.340
370	39.30	6.26	0.10	39.00	0.1040	4.060
373	39.60	6.30	0.04	39.45	0.0495	1.955
376	40.00	6.38	0.08	39.80	0.0855	3.400
379	40.20	6.41	0.03	40.10	0.0425	1.710
382	40.20	6.41	0.00	40.20	0.0300	1.210
385	39.50	6.30	0.11	39.85	0.1140	4.550
388	38.80	6.18	0.12	39.15	0.1235	4.840
391	38.50	6.13	0.05	38.65	0.0580	2.240
					Total =	47.60 sq. cm.
			C. Every Fourth Section			
352	34.90	5.55	0.00	34.90	0.0400	1.395
356	35.70	5.70	0.15	35.30	0.1550	5.480
360	36.90	5.88	0.18	36.30	0.1840	6.680
364	37.70	6.01	0.13	37.30	0.1390	5.200
368	39.00	6.21	0.20	38.85	0.2035	7.900
372	39.50	6.29	0.09	39.25	0.0985	3.870
376	40.00	6.38	0.09	39.75	0.0985	3.915
380	40.20	6.41	0.03	40.10	0.0500	2.010
384	40.00	6.38	0.03	40.10	0.0500	2.010
388	38.80	6.18	0.20	39.40	0.2035	8.050
392	38.60	6.15	0.03	38.70	0.0500	1.935
					Total =	48.54 sq. cm.

TABLE 7.—*Visible Surface Area of Cerebrum in Forty-One Consecutive Sections, Showing that Measuring Only Every Tenth Section Does Not Introduce Any Error of Importance—Continued*

Visible Surface Areas of Cerebrum in Forty-One Sections to Determine the Interval Between Sections at Which an Appreciable Error Will Occur

Section Number	Perimeter (Cm.)	r (Cm.)	$r-r_1$ (Cm.)	$\frac{A+B}{2}$ (Cm.)	s (Cm.)	$s \times \frac{A+B}{2}$ (Sq. Cm.)
			D. Every Fifth Section			
352	34.90	5.55	0.00	34.90	0.0500	1.750
357	36.00	5.75	0.20	35.95	0.2055	7.500
362	37.20	5.93	0.18	36.60	0.1862	6.820
367	38.70	6.16	0.23	37.95	0.2350	8.950
372	39.50	6.29	0.13	38.60	0.1385	5.350
377	40.10	6.40	0.11	39.30	0.1200	4.725
382	40.20	6.41	0.01	40.15	0.0140	0.580
387	39.20	6.24	0.15	39.70	0.1580	6.280
392	38.60	6.15	0.09	38.90	0.1028	4.120
						Total = 46.09 sq. cm.
			E. Every Sixth Section			
352	34.90	5.55	0.00	34.90	0.0600	2.098
358	36.30	5.80	0.25	35.60	0.2565	9.150
364	37.70	6.01	0.21	37.00	0.2180	8.060
370	39.30	6.26	0.25	38.50	0.2565	9.900
376	40.00	6.38	0.12	39.35	0.1338	5.552
382	40.20	6.41	0.03	40.10	0.0620	2.480
388	38.80	6.18	0.23	39.50	0.2370	9.370
						Total = 46.60 sq. cm.
			F. Every Seventh Section			
352	34.90	5.55	0.00	34.90	0.0700	2.480
359	36.60	5.82	0.27	35.75	0.2800	10.000
366	38.40	6.12	0.30	37.50	0.3080	11.580
373	39.60	6.30	0.18	39.00	0.1925	7.520
380	40.20	6.41	0.11	39.90	0.1300	5.200
387	39.20	6.26	0.15	39.70	0.1655	6.580
						Total = 43.38 sq. cm.
			G. Every Eighth Section			
352	34.90	5.55	0.00	34.90	0.800	2.780
360	36.90	5.88	0.33	35.90	0.3410	12.400
368	39.00	6.21	0.33	37.95	0.3410	13.300
376	40.00	6.38	0.17	39.50	0.1875	6.600
384	40.00	6.38	0.00	40.00	0.0800	3.200
392	38.60	6.15	0.23	39.30	0.2425	9.550
						Total = 47.83 sq. cm.
			H. Every Ninth Section			
352	34.90	5.55	0.00	34.90	0.0900	3.18
361	37.00	5.90	0.35	35.95	0.3610	13.00
370	39.30	6.26	0.36	38.15	0.3700	14.10
379	40.20	6.41	0.15	39.75	0.1745	6.93
388	38.80	6.18	0.23	39.50	0.2465	9.10
						Total = 46.31 sq. cm.
			I. Every Tenth Section			
362	37.20	5.93	0.43	36.05	0.4410	15.90
372	39.50	6.29	0.36	38.35	0.3725	13.80
382	40.20	6.41	0.12	39.85	0.1560	6.05
392	38.60	6.15	0.26	39.40	0.2775	10.90
						Total = 46.65 sq. cm.

TABLE 8.—*Perimeter for Total Area of Brain Cut Horizontally—Every Tenth Section*

Section	Right (Cm.)	Left (Cm.)	Section	Right (Cm.)	Left (Cm.)
860	9.50	9.50	450	72.50	61.50
850	9.50	9.50	440	60.50	52.50
840	14.90	31.40	430	49.50	90.00
830	32.70	46.50	420	88.00	92.00
820	51.50	52.50	410	79.00	97.00
810	74.50	57.00	400	85.00	104.50
800	77.50	66.00	390	88.00	104.50
790	85.00	91.00	380	88.50	109.00
780	87.00	90.00	370	70.50	80.00
770	74.00	94.50	360	91.50	84.00
760	75.00	97.50	350	72.00	85.00
750	81.50	97.50	340	62.50	71.00
740	91.50	96.50	330	70.00	68.00
730	101.00	90.70	320	63.00	63.00
720	102.00	95.00	310	53.00	55.00
710	98.00	90.50	300	49.50	48.30
700	90.50	90.00	290	55.00	46.50
690	84.00	86.00	280	55.00	60.50
680	92.00	83.20	270	55.00	62.00
670	94.00	77.50	260	51.00	62.00
660	94.00	87.30	250	51.00	62.50
650	94.50	81.00	240	46.00	50.50
640	92.00	86.50	230	41.50	46.00
630	85.50	83.50	220	28.60	36.80
620	91.50	90.00	210	30.50	32.50
610	88.50	78.50	200	24.60	31.00
600	88.00	79.50	190	21.40	29.50
590	88.00	81.00	180	21.40	30.50
580	81.50	81.00	170	21.40	24.40
570	86.00	87.00	160	22.00	22.00
560	91.50	92.00	150	22.00	22.00
550	93.50	104.00	140	17.70	20.60
540	95.00	95.50	130	14.00	18.00
530	86.50	96.00	120	9.90	15.40
520	99.00	107.50	110	9.25	13.70
510	64.00	100.00	100	7.85	9.45
500	35.60	77.00	90	3.75	6.80
490	35.60	64.00	50	1.40	2.40
480	35.60	19.30	40	1.20	2.06
470	16.70	37.80			
460	34.00	65.00	79 sections =	4754.95 cm.	5117.75 cm.
			Average section =	60.16 cm.	64.77 cm.

TABLE 9.—*Visible Surface Area of Cerebrum (Calculated as the Sum of the Frusta of Truncated Cones)—Between Every Ten Sections*

Section Number	Perimeter (Cm.)	Radius (Cm.)	$r-r_1$ (Cm.)	$\frac{A+B}{2}$ (Cm.)	s (Cm.)	S (Sq. Cm.)
860	5.92	0.942	0.942	2.90	0.943	2.79
850	15.82	2.515	1.573	11.37	1.573	17.90
840	17.75	2.820	0.320	15.78	0.320	5.36
830	20.80	3.310	0.490	19.33	0.498	9.65
820	21.65	3.450	0.140	20.23	0.172	3.48
810	22.80	3.620	0.170	22.23	0.195	4.33
800	24.65	3.920	0.300	23.73	0.315	7.47
790	25.10	3.990	0.070	24.88	0.119	2.96
780	25.50	4.060	0.070	25.30	0.119	3.01
770	23.00	3.660	0.400	24.25	0.472	10.00
760	21.95	3.490	0.170	22.48	0.195	4.39
750	20.25	3.220	0.290	21.10	0.305	6.44
740	20.20	3.210	0.010	20.23	0.101	2.04
730	19.90	3.170	0.040	20.05	0.107	2.15
720	21.90	3.480	0.310	20.80	0.324	6.77
710	24.10	3.830	0.350	23.00	0.361	8.70
700	25.25	4.010	0.180	24.68	0.205	5.17
690	25.80	4.100	0.090	25.53	0.134	3.46
680	25.75	4.090	0.010	25.78	0.101	2.60
670	24.55	3.900	0.190	25.15	0.214	5.37
660	24.05	3.820	0.080	24.30	0.127	3.09
650	25.30	4.020	0.200	24.68	0.223	5.50
640	26.50	4.210	0.190	25.90	0.214	5.54

TABLE 9.—*Visible Surface Area of Cerebrum (Calculated as the Sum of the Frusta of Truncated Cones)—Between Every Ten Sections—Continued*

Section Number	Perimeter (Cm.)	Radius (Cm.)	r-r_1 (Cm.)	$\frac{A+B}{2}$ (Cm.)	s (Cm.)	S (Sq.Cm.)
630	31.30	4.970	0.760	28.90	0.762	22.00
620	34.00	5.410	0.440	32.65	0.451	14.72
610	34.30	5.450	0.040	34.15	0.107	3.65
600	35.65	5.660	0.210	34.98	0.230	8.04
590	37.90	6.020	0.360	36.78	0.370	13.59
580	33.90	5.380	0.640	35.90	0.643	23.10
570	33.25	5.280	0.100	33.58	0.141	4.73
560	30.35	4.830	0.450	31.30	0.456	14.25
550	33.10	5.260	0.370	31.73	0.378	12.00
540	32.80	5.210	0.050	32.95	0.112	3.68
530	32.30	5.130	0.080	32.55	0.127	4.14
520	35.95	5.710	0.580	33.63	0.586	19.73
510	35.45	5.640	0.070	35.70	0.119	4.25
500	34.80	5.530	0.110	35.13	0.147	5.17
490	33.70	5.350	0.180	34.25	0.205	7.08
480	34.20	5.430	0.080	33.95	0.127	4.30
470	36.00	5.720	0.290	35.10	0.305	10.70
460	35.70	5.670	0.050	35.85	0.112	4.03
450	37.80	6.000	0.330	35.75	0.342	12.20
440	36.40	5.940	0.060	37.10	0.116	5.95
430	38.60	6.130	0.190	37.50	0.214	8.04
420	39.40	6.260	0.130	39.00	0.164	6.40
410	39.44	6.270	0.010	39.42	0.101	3.95
400	38.40	6.100	0.170	38.92	0.195	7.58
390	40.10	6.370	0.270	39.25	0.187	7.35
380	40.40	6.420	0.050	40.25	0.112	4.52
370	39.10	6.210	0.210	39.75	0.230	9.11
360	35.40	5.630	0.580	37.25	0.586	21.42
350	34.40	5.470	0.160	34.90	0.187	6.55
340	34.90	5.550	0.080	34.65	0.127	4.40
330	32.95	5.240	0.310	33.93	0.324	11.30
320	32.95	5.240	0.000	32.95	0.100	3.29
310	34.00	5.410	0.170	33.48	0.195	6.55
300	32.35	5.130	0.280	34.18	0.296	10.20
290	33.70	5.360	0.230	33.03	0.249	8.25
280	36.10	5.740	0.380	34.90	0.389	13.60
270	32.70	5.200	0.540	34.40	0.547	18.84
260	31.85	5.060	0.140	32.33	0.172	5.56
250	30.20	4.800	0.260	31.08	0.277	7.68
240	29.80	4.730	0.070	30.00	0.119	5.70
230	28.00	4.450	0.280	28.90	0.296	8.55
220	26.90	4.270	0.180	27.45	0.205	5.64
210	25.95	4.130	0.140	26.43	0.172	4.56
200	25.00	3.970	0.160	25.48	0.182	4.77
190	24.30	3.860	0.170	24.65	0.195	4.82
180	21.40	3.400	0.460	22.85	0.468	10.70
170	21.65	3.440	0.040	21.53	0.107	2.31
160	20.65	3.300	0.140	21.15	0.172	3.64
150	18.15	2.880	0.420	19.40	0.428	8.32
140	20.20	3.210	0.330	19.18	0.343	6.58
130	15.30	2.430	0.780	17.70	0.783	13.85
120	13.70	2.180	0.250	14.50	0.268	3.74
110	11.15	1.770	0.410	12.43	0.429	5.34
100	8.17	1.330	0.470	9.66	0.478	4.62
90	4.13	0.660	0.640	6.15	0.644	3.96
50	2.76	0.440	0.220	3.45	0.240	0.82
40	2.76	0.440	0.000	2.76	0.100	0.28
			Total =	2183.86		586.41 sq.cm.
			Average $\frac{A+B}{2}$ =	27.64		

TABLE 10.—*Surface Area of Human Cerebrum*

		Surface Without Shrinkage (Sq. Cm.)	Surface With Shrinkage, 9 per Cent (Sq. Cm.)	Average $\frac{A+B}{2}$ (Cm.)	Ratio of the Perimeters of Visible and Total Surface
Visible surface area	Right	293.20	319.59	13.77	4.36 : 1
	Left	293.20	319.59	13.76	4.70 : 1
	Total	586.40	639.18	27.53	4.53 : 1
Total surface area	Right	1278.35	1393.40	60.16	1 : 4.36
	Left	1378.04	1502.06	64.77	1 : 4.70
	Total	2656.39	2895.46	124.93	1 : 4.53

Calculation of One Entire Cerebrum.—The method outlined was applied to the entire cortical surface by measuring and calculating every tenth section. Our calculations show that the visible surface area is 586.40 sq. cm. without considering shrinkage, and 639.18 sq. cm. when shrinkage is considered.

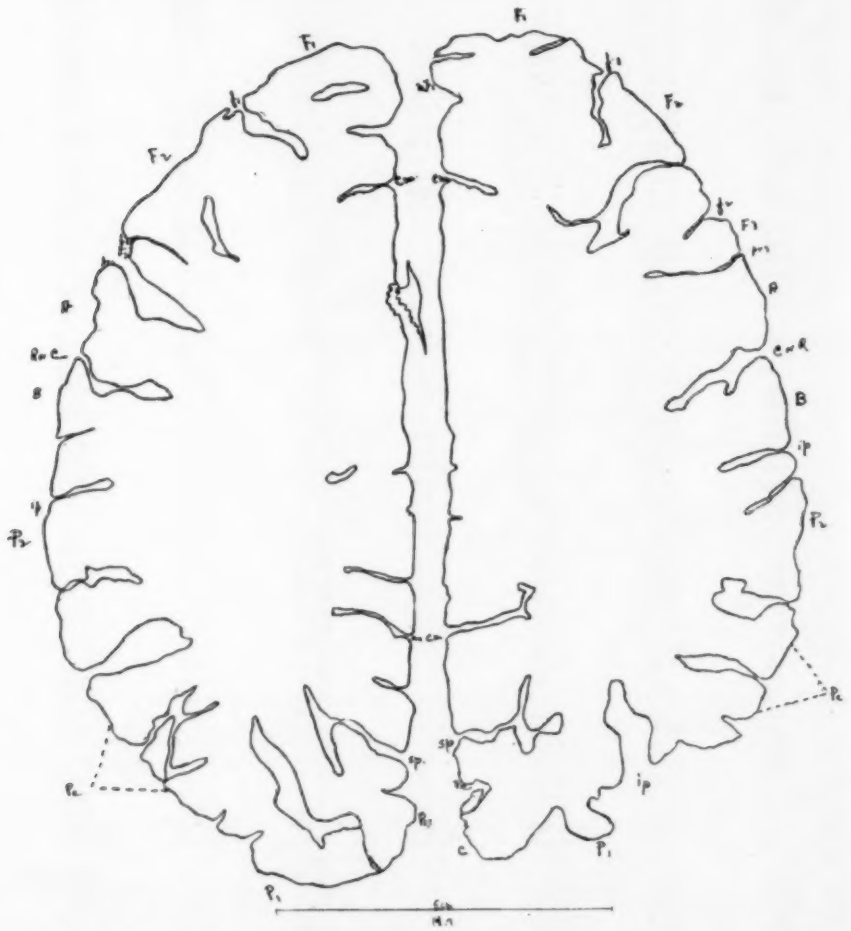

Fig. 12.—Contour of horizontal section of the cerebrum taken at a distance of 2 cm. from the vertex (section 620).

The perimeter or average $\frac{A+B}{2}$ for the total visible surface is 27.64 cm. (table 9), for the total surface of both hemispheres, 124.93 cm. (table 8). The average $\frac{A+B}{2}$ for the right visible surface was 13.77 cm., for the left visible perimeter 13.76 cm. (tables 8 and 10). The average $\frac{A+B}{2}$ for the right total perimeter is 60.16 cm., for the left total perimeter 64.77 (tables 8 and 10).

The ratios of these different areas are given in table 10. For the entire cerebral surface we find a ratio of 4.53 between the total and the visible surfaces. The right hemisphere has a ratio of total to visible surface of 4.36:1 and the left hemisphere, a ratio of 4.70:1. By comparing these ratios to those in table 6 (of the forty-one consecutive

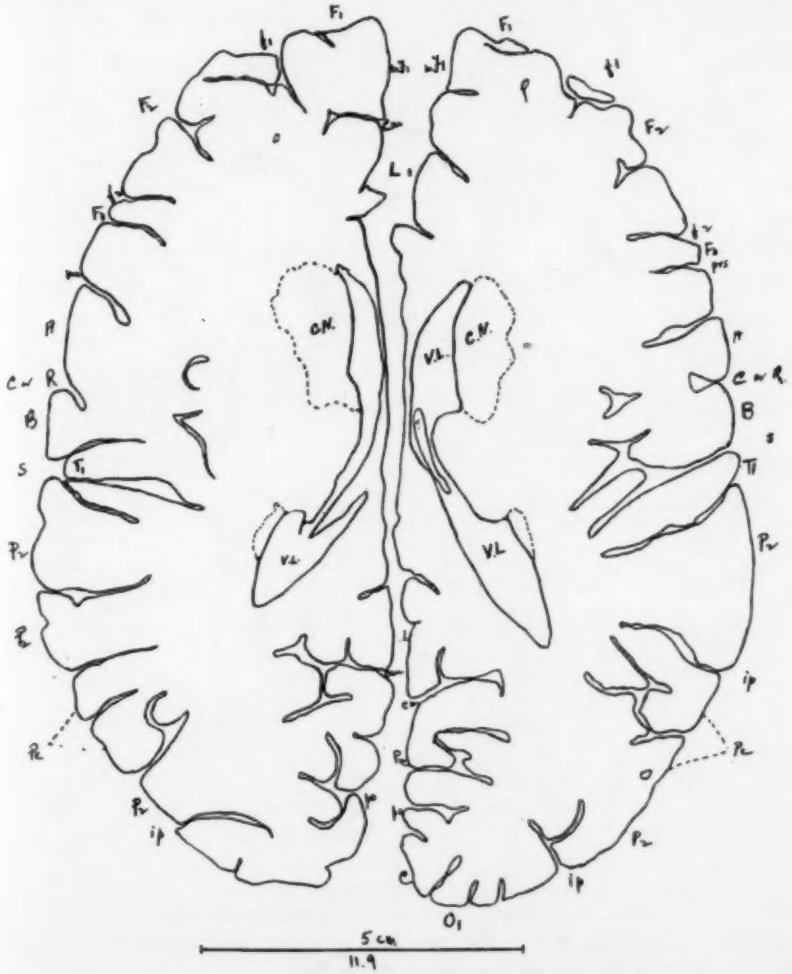

Fig. 13.—Contour of horizontal section of the cerebrum taken at the level of the lateral ventricle (section 520).

sections), it may be seen how close they are. The ratio for the forty-one consecutive sections is somewhat larger, for this area does not include some of the smaller areas of the brain.

Our calculations of the total surface of the cerebrum give a result of 2,656.39 sq. cm., when shrinkage is not considered and 2,895.46

sq. cm. when shrinkage is added. The right hemisphere is 1,393.40 sq. cm. and the left hemisphere, 1,502.05 sq. cm. The visible surfaces and all the ratios are given in table 10.

There were certain conspicuous differences in the surfaces between sections. In order to determine the reason for these variations, we made drawings and graphs of sections. Figure 6 shows the relation of

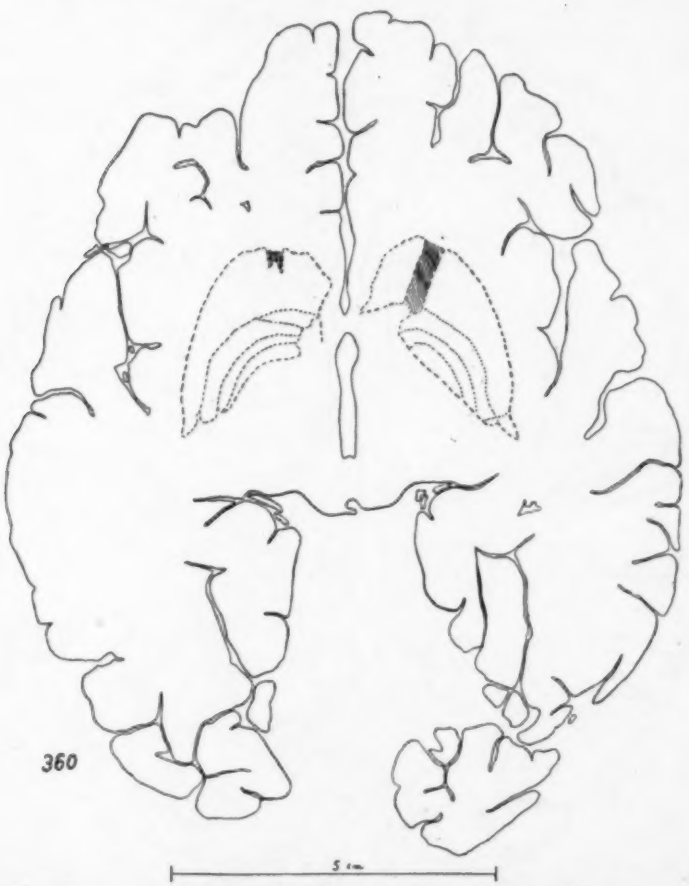

Fig. 14.—Contour of horizontal section of the cerebrum taken at the level of the cerebellum (section 360). The presence of the cerebellum accounts for the variations in the perimeter, as mentioned in the text.

the visible surface, without the median longitudinal fissure, to the total surface. Figure 8 shows the relation of the visible surface plus the median longitudinal fissure to the total surface. Figure 9 is a combination of figures 6 and 8 and shows the percentages of the visible surfaces in relation to the total surface area. The contours of the brain (figs. 10, 11, 12, 13, 14, 15 and 16) show definitely why the outlines in the graphs showed certain irregularities. From these figures, one can readily

see that the variations occur at about the level of the vertex of the brain, in the middle portion of the cerebrum between sections 540 and 440, and 350 and 230 (figs. 6 and 8).

The reasons for these apparent discrepancies are as follows: In the first sections the marked apparent discrepancies are due to the marked slanting of the cortex at the vertex and the lack of fissures. Between

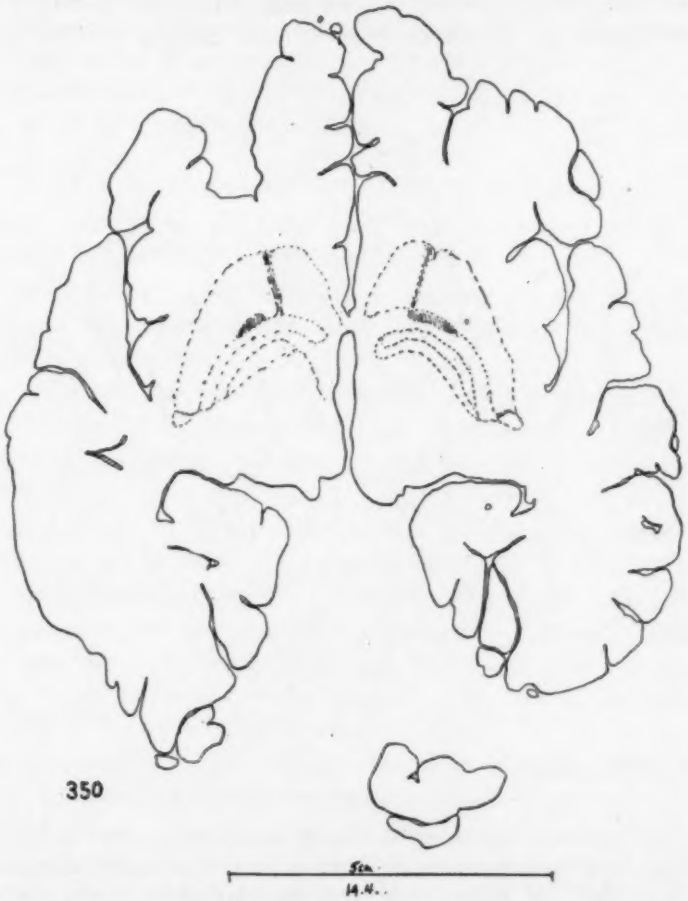

Fig. 15.—Contour of horizontal section of the cerebrum following figure 14 (section 350) to show the abrupt variation in the perimeter produced by the separation of the occipital pole from the cerebrum by the cerebellum.

sections 540 and 440, the great variations were due to the fact that in this place the brain was cut in two halves and mounted as two separate blocks. The last scetions of the first block and the first sections of the second block were uneven and broken. At section 350, the presence of the cerebellum accounts for the new variations. At section 230 the

suddenness in change of the figures is due to the same cause as at the beginning on the sections i.e., the marked slanting of the cortex and the lack of fissures.

COMMENT

In comparison with the results of Henneberg, Wagner, etc., we find that our figures are somewhat larger. The cerebrum which we measured may have a greater surface area than those measured by the authors mentioned. However, after careful analysis we feel that the

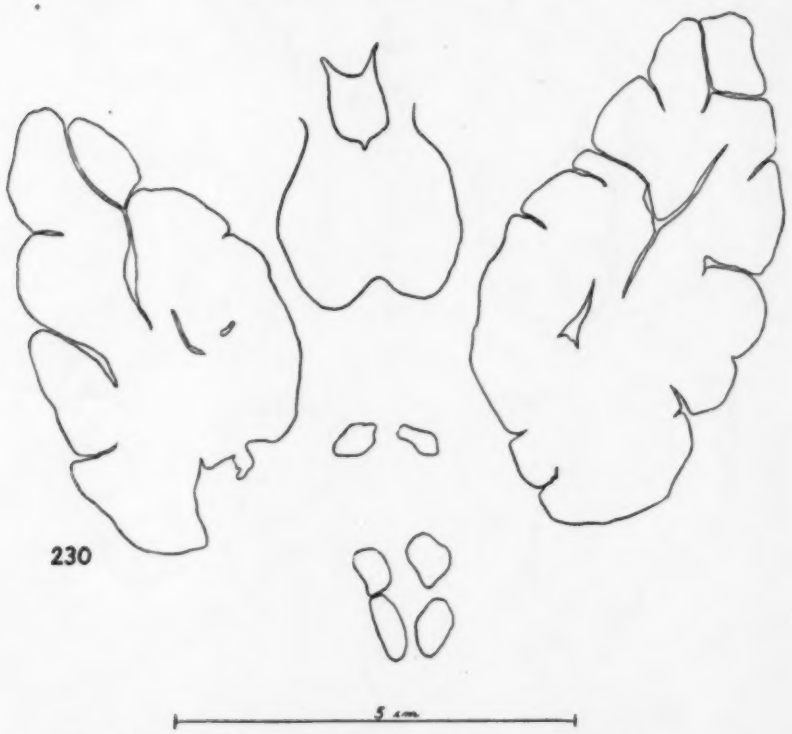

Fig. 16.—Contour of horizontal section of the cerebrum taken at about two thirds of the distance from the vertex (section 230), showing the absence of the cerebellum. Below this section there is an abrupt decrease in the size of the perimeter.

method of procedure had a great deal to do with the larger figures in our case. The authors mentioned did not consider shrinkage as a factor. The sections they used were much thicker, being 1 cm. instead of 100 microns thick, and were not projected and not enlarged. If the contour of a section is observed, it is evident that the smaller and deeper fissures could not be reached accurately except by a fine measuring device. The ratio between the visible and total surface area found by Henneberg was 1 : 2.94. Evidently he took into consideration the visible surface includ-

ing the median longitudinal fissure. Using the same visible surface, we found about the same ratio (fig. 8).

To convince ourselves of this, we measured the cerebral surface in a way somewhat similar to that of Henneberg. The cerebral hemispheres were broken up along the fissures into small pieces, and each piece was measured and calculated according to the geometric form assumed. The following results were obtained: The visible surface without the median longitudinal fissure was 616.20 sq. cm.; the visible area with the median longitudinal fissure was 687 sq. cm., as compared to 717 sq. cm. found by Henneberg. The total surface was 2,212 sq. cm. The total surface found by Henneberg was 2,262 sq. cm.

GENERAL COMMENT ON SOURCES OF ERROR

Following is a list of elements of error. Some of these can be eliminated, while others are unavoidable.

Shrinkage.—During the different processes of embedding, there is shrinkage of the volume of the brain. This loss was taken into consideration in our method.

Thickness of Sections.—The sections are not always cut uniformly by the microtome. The first sections are usually thicker. This can be eliminated if the cutting is done continuously and the brain deeply embedded.

Projection.—Even though the sections are enlarged, some of the small sulci cannot be seen. This can be eliminated by rechecking with a hand lens when the sections are redrawn on white paper with India ink.

Measurement by the Aid of the Measuring Device.—Measuring devices have to be checked from time to time as they may not register properly. The measuring device we use at present is not graded in millimeters. This adds to the error.

The Formula and Calculations.—We are not dealing with a truncated cone, geometrically speaking.

Determination of Visible Area.—Visible area is an arbitrary term. We considered the visible area as that area of the cerebrum which may be seen after the cerebellum and pons are removed. We did not consider the median longitudinal fissure as visible area.

CONCLUSIONS

We have attempted to give an idea of the principles, the necessary technic and the elements of error, some of which can be avoided and some of which cannot. We present some tentative figures in the estimation of the cerebral cortical surface. According to this method, the total cerebral surface was found to be 2,895.40 sq. cm.; the visible cerebral surface, 639.18 sq. cm., giving as a ratio 4.53:1.

INFLUENCE OF MALARIAL TREATMENT ON THE SPINAL FLUID IN GENERAL PARALYSIS *

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I shall report data to illustrate the influence of malaria treatment, without subsequent arsenical therapy, on the spinal fluid observations in general paralysis. These data consist of observations on: the cell count in ninety cases, quantitative determinations of the total protein in the spinal fluid in sixteen cases in which the patients were treated recently and in thirty-eight patients under observation for two years or longer subsequent to treatment, and quantitative determinations of the Wassermann reaction in the spinal fluid in forty-seven cases over a post-treatment period of from two to three and three-fourths years. The Vernes test [1] has been applied in the majority of these cases, and this will form the subject of a future communication. The results are reported without reference to the work of others; of the latter, a comprehensive bibliography will be found in the recent article of Ferraro and Fong.[2]

CELL COUNT

A definite reduction in the cell count, usually to a normal value, occurred in eight-three of ninety cases, or in 92 per cent, which exhibited a pleocytosis prior to treatment. In three of the eighty-three, the reduction was only temporary; it was found at the initial examination, subsequent to the course of malaria, with the reappearance of a pleocytosis on examination one month later and thereafter. In sixty-five of the eighty-three cases, the reduction in the cell count to normal (5 cells per cubic millimeter or less) or almost normal (from 6 to 10 cells per cubic millimeter) was demonstrable within a week of the final malarial paroxysm; in the remaining eighteen, this took a month or longer to accomplish, a normal cell count having been found for the first time six months subsequent to the final malarial paroxysm in four patients, at the end of three months in four and at the end of one month in the remaining ten cases. Thus, sixty-five of ninety patients (72 per cent) exhibited an immediate reduction in the cell count to normal following treatment; in ten additional patients, (11 per cent) this response

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* From the New York State Psychiatric Institute, Ward's Island.

1. Cornwall, L. H.: The Vernes Reaction: Technic and Preliminary Experiences, Arch. Dermat. & Syph. **5**:433 (April) 1922.

2. Ferraro, A., and Fong, T. C. C.: The Serology of General Paresis in the Malaria Treated Cases, New York M. J. **124**:562, 607 and 682 (Nov. 3 and 17 and Dec. 1) 1926.

required a month to manifest itself; in fifteen patients (17 per cent), the reduction in the cell count was still further delayed or did not occur. Mere delay in the modification of the meningeal reaction appears to be without any conclusive bearing on the clinical outcome. However, of the seven patients in whom little if any modification of the pleocytosis took place during a post-treatment period of from three months to four years, three died at the end of from three to eighteen months. In one patient, who exhibited a low grade pleocytosis throughout the course of the disease (never below from 8 to 11 cells per cubic millimeter), a clinical relapse occurred after an excellent remission lasting three years and three months, accompanied by a further rise in the cell count (to 35) and a notable increase in the total protein of the spinal fluid.[3] In the remaining three patients, treatment with tryparsamide, which was begun from seven to fourteen months after the malaria treatment, terminated the pleocytosis, which in one of the cases also accompanied a beginning retrogression from a state of fairly well marked clinical improvement. In two of the seven patients, in addition to the case just described, a definite if temporary clinical improvement was likewise not inconsistent with the persistence of a rather marked pleocytosis; in one patient, this took place in the presence of a pleocytosis of from 27 to 120 cells per cubic millimeter, which persisted until death eighteen months subsequent to malaria. In the second patient, still living after twenty-six months and now slowly declining, a temporary mental improvement of definite degree occurred despite a continuous pleocytosis of from 12 to 56 cells per cubic millimeter. Thus the relationship, if there is any, between a persistent pleocytosis and the therapeutic result does not appear clearly; the data suggest the possibility, however, that such a phenomenon augurs an unsatisfactory clinical outcome, although the mere postponement of a cytologic return to normal, certainly if for not more than one month after completing treatment, does not seem to preclude a favorable issue from the standpoint of mental improvement or remission.[4]

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3. Bunker, H. A., Jr., and Kirby, G. H.: The Treatment of General Paralysis by Inoculation with Malaria: III. Fourth-Year Results, J. A. M. A., to be published.

4. I have elsewhere (Bunker, H. A., Jr., and Kirby, G. H.: The Treatment of General Paralysis by Inoculation with Malaria: A Second Report, Arch. Neurol. & Psychiat. **16**:182 [Aug.] 1926) reported the case (case 8) of a patient in whom an extremely complete clinical remission following malaria set in with promptitude, but in whom the cell count rose steadily (to 117 per cubic millimeter at the end of four months) after an initial reduction immediately after treatment to practically normal (4 per cubic millimeter). Tryparsamide treatment was then instituted on the assumption that to withhold it would seriously endanger the patient's welfare. The pleocytosis disappeared at once, and the patient, who has now received a total of seventy injections of tryparsamide, remains in excellent condition after an interval of three years since the course of malaria.

ALBUMIN CONTENT

For the quantitative determination of the albumin content of the spinal fluid I have employed the rapid clinical method recently suggested by Young and Bennett,[5] which I have found simple, convenient and trustworthy.[6] Because the values ranged from 10 to 55 mg. per hundred cubic centimeters (average, 36 mg.), in eight nonsyphilitic control cases, I am in general agreement with the statement of these writers that, with their method, a reading up to 75 mg. may be regarded as falling within essentially normal limits—from 50 to 75 mg. being a "high normal" and from 75 to 100 mg. a borderline value, according to their interpretation.

In twenty-two cases of general paralysis in which the patients were examined prior to malaria treatment, the values ranged from 65 to 425 mg. per hundred cubic centimeters, the average reading for the twenty-two being 192 mg.[7] Nine of these patients had, it is true, received arsphenamine intravenously, usually a moderate amount, prior to admission to the hospital. This circumstance is probably responsible for the fact that eight of these, with values of from 65 to 125 mg. of albumin, represent the eight lowest readings in the group, the minimum content for an untreated patient being 145 mg. and the average for the thirteen untreated patients being 245 mg.

More or less analogous to the behavior of the cell count, in all but four of sixteen patients who received the malaria treatment, immediately subsequent to the course of fever there was a definite and often material reduction in the albumin content of the spinal fluid so that the average reading, directly after the course of malaria, was 156 mg. in these sixteen cases (ranging from 85 to 245 mg.), as compared with an average of 192 mg. before treatment with malaria. Furthermore, seven of the thirteen patients examined after the lapse of one month exhibited a still further reduction in the total albumin; the seven included three of the four who had not shown any reduction immediately after treatment. Thus, in thirteen patients the average albumin content at the end of one

5. Young, G. A., and Bennett, A. E.: Studies on the Quantitative Estimation of the Total Protein Content in Cerebrospinal Fluid, Am. J. M. Sc. **172**:249 (Aug.) 1926.

6. My colleagues and I have found it of importance to test the inner surface of the junction of the body of the vaccine tube with the capillary portion, as with a wooden applicator, for example. In our experience, a definite degree of roughening or lipping at this junction seems to have the effect of retaining a small amount of the precipitated albumin and so of somewhat reducing the total quantity thrown down into the capillary portion on centrifugalization.

7. Young and Bennett obtained readings varying from 87 to 500 mg. with an average of 200 mg. per hundred cubic centimeters in fifty-seven cases of general paralysis.

month from the completion of treatment with malaria was 124 mg. (ranging from 65 to 240 mg.). Finally, among those who had been treated recently and whose cases were followed up for three months, five showed a still further reduction in the albumin content and five did not; thus, in these ten patients the average albumin content at the end of three months from the completion of treatment with malaria, was 91 mg. with a range of from 50 to 125 mg. The rather definite character of this diminution in the amount of total protein in the spinal fluid soon after treatment is made evident in table 1.

As in the case of the cell count, then, it is clear that malaria treatment produces a tendency toward a distinct diminution in the albumin content of the spinal fluid—a tendency which expresses itself unequivocally at the end of one month, rather than immediately after treatment, but which in a few cases is not definitely observable until three months from the time of completing the course of malaria treatment.

TABLE 1.—*Influence of Malaria on Albumin Content of Spinal Fluid*

	Average, Mg. per 100 Cc.	Range, Mg. per 100 Cc.
Prior to malaria	192	65-425 (22 cases)
Immediately after malaria	156	85-240 (16 cases)
One month after malaria	124	65-240 (13 cases)
Three months after malaria	91	50-125 (10 cases)

In only eleven of a group of thirty-eight patients under observation for a period of two years or longer since treatment with malaria is the albumin content of the spinal fluid now 75 mg. or higher; in sixteen, it is 50 mg. or lower. Hence, after from two to three and one-half years, 42 per cent of these patients have a practically normal amount of total protein in the spinal fluid, 29 per cent give a "high normal" reading and 29 per cent show an albumin content which is still somewhat increased. The sixteen patients with a normal albumin content have an average of 42 mg. (ranging from 25 to 50 mg.); the eleven patients with a "high normal" albumin, an average of 61 mg., and the eleven patients with a definitely elevated albumin content, an average of 85 mg. (ranging from 80 to 195 mg.); the total protein is above 100 mg. in only three patients of the last group, one of whom had a high reading (195 mg.) on the occasion of a clinical relapse from a full remission of three years' standing.[3]

Apart from the fact that of the three patients whose total protein is still in excess of 100 mg. at the end of a period of from two to more than three years, two present stationary and unimproved cases while the third has (as just noted) a relapse from a state of remission, there appears to be no definite relationship between the behavior of the total protein in the spinal fluid and the therapeutic outcome. Six of sixteen

patients whose spinal fluid has a present normal protein content of 50 mg. or below are mentally unimproved; conversely, four of eleven patients whose spinal fluid continues to show a total protein of from 80 to 100 mg. have had full remission of their condition for at least two years. It would seem that the mere lapse of time played the major part in bringing about a reduction in the albumin content of the spinal fluid subsequent to malaria treatment, at least in the majority of cases. Of the nineteen patients in whom the albumin in the spinal fluid has been determined at the end of three or three and one-half years, ten belong in the normal group, six in the "high normal" group and only three in the abnormal group; whereas of the nineteen patients for whom this determination has been made after a lapse of two or two and one-half years, only six belong in the normal, five in the "high normal" and eight in the abnormal group. In summarizing, there is merely the negative indication that an eventual reduction in the albumin content is not a reflection of the clinical progress or status of the patient; a persistent reading in excess of 100 mg. or a subsequent return to that level seems, on the other hand, to be inconsistent with a satisfactory or enduring therapeutic result. It is also well to recall, perhaps, that in these thirty-eight patients the malaria treatment presumably has not been without some effect, since all have now lived for a period materially in excess of the average expectancy of life (one and one-half years) of patients with general paralysis in state hospitals.[8] As these patients are in this sense a selected group, there is perhaps somewhat less reason for denying in these cases all parallelism between therapeutic effect and reduction in the spinal fluid protein.[9]

THE WASSERMANN REACTION IN THE SPINAL FLUID

The degree of positivity of the Wassermann reaction [10] in the spinal fluid at the end of a period of from two years to three years and nine

8. Pollock, H. M.: Annual Statistical Review of the Patients Treated in the State Hospitals and Private Licensed Institutions for Mental Disease, Albany M. Ann., 1925, p. 224.

9. One may refer here, parenthetically, to the statement of Kaltenbach (Kaltenbach, H.: Ueber einige prognostiche Schlüsse aus den Liquoranalysen bei malariabehandelten Paralytikern, Arch. f. Psychiat. **71**:384, 1924.) that in his experience those patients offer the best prognosis who exhibit a low phase I reading prior to treatment. The data available on recently treated patients in this clinic do not appear to support this statement clearly, but they are insufficient to controvert it.

10. It should be stated that all the patients here dealt with gave positive results with 0.2 cc. of spinal fluid prior to malaria treatment. The Wassermann technic of the New York State Department of Health—sheep system, with four hour icebox fixation—has been employed.

months in forty-seven patients who did not receive supplementary antisyphilitic treatment subsequent to malaria, is indicated in table 2.

That almost one half of these patients should eventually exhibit a marked reduction in the strength of the Wassermann reaction in the spinal fluid is sufficiently remarkable, and that nearly one fourth of the reactions should become completely negative seems even more so, when it is considered that general paralysis represents the Wassermann-fast condition par excellence, that prolonged intravenous treatment with arsphenamine is rarely effective against a positive Wassermann test of the spinal fluid and that a large number of intraspinal injections of arsphenaminized serum, or of seventy-five or one hundred injections of tryparsamide,[11] are almost invariably required to render the reaction negative in this disease, even in the few cases in which this result can be obtained.

TABLE 2.—*Influence of Malaria on the Wassermann Reaction in the Spinal Fluid*

	1.0 Cc.	0.5 Cc.	0.2 Cc.	Number	Per Cent	
Unchanged				19	40	
Acetone-insoluble antigen	++++	++++	++ to ++++			26
Cholesterol antigen	++++	++++	++++			
Modified				7	15	
Acetone-insoluble antigen	++++	++ to ++++	Negative			
Cholesterol antigen	++++	++ to ++++	Negative			
Much modified				11	24	
Acetone-insoluble antigen	++ to ++++	Negative	Negative			21
Cholesterol antigen	++++	Neg. to ++	Negative			
Negative				10	21	
Acetone-insoluble antigen	Negative	Negative	Negative			
Cholesterol antigen	Neg. to ++	Negative	Negative			

Before noting the relation between the serologic and the therapeutic outcome in these cases, reference may be made to the length of time required to reach the status of the spinal fluid Wassermann test reported in table 2. The seven patients presenting a slight though definite modification in the strength of the Wassermann reaction first exhibited the degree of modification now present after a period of from one to two years subsequent to malaria treatment—three after one year, one after eighteen months, one after twenty-one months and two after two years. In nine of the eleven patients now presenting a marked modification in the strength of the spinal fluid Wassermann reaction, this degree of change first became evident from one and one-fourth to two and one-half years after treatment; in the remaining two, this interval was nine

11. Solomon, H. C., and Viets, R. H.: Tryparsamide Treatment of Neurosyphilis: Second Report, J. A. M. A. **85**:329 (Aug. 1) 1925. Bunker, H. A., Jr.: The Effect of One Hundred Injections of Tryparsamide on the Spinal Fluid in General Paralysis, Am. J. M. Sc., to be published.

months and one year, respectively. Two of the ten patients now giving negative reactions first did so at eighteen months after treatment, one at twenty-five months, four at two years and two at thirty-three months. Table 3 presents the total situation, which seems to contain the suggestion that a further lapse of time would bring about a still further modification in the Wassermann reaction in the spinal fluid, at least in some instances. Five of the seven patients in the first column (table 3), however, have persisted in their present status for a year or longer, and the same is true of six of the eleven patients in the second column; yet it cannot be said a priori, even though at least two and one-half years have elapsed in the case of most of these patients since the course of treatment with malaria, that the possibility of a future further reduction in the Wassermann reaction is out of the question.

Of the nineteen patients in whom essentially no modification of the Wassermann reaction has taken place in the course of from two to three

TABLE 3.—*Wassermann Modification in Relation to Interval Since Malaria*

Interval Subsequent to Malaria Necessary to Attain Degree of Modification Now Present	Modified	Much Modified	Negative	Total
Three months	0	0	1	1
Nine months	0	1	0	1
One year	3	1	0	4
Fifteen months	0	1	0	1
Eighteen months	1	3	2	6
Twenty-one months	1	0	1	2
Two years	2	4	4	10
Thirty months	0	1	0	1
Thirty-three months	0	0	2	2
	7	11	10	28

and one-half years since treatment, one died two years and a half subsequent to treatment with malaria; seven, though still living, exhibit essentially no mental improvement, yet do not appear to have retrogressed during this interval; one suffered a partial relapse after an excellent remission of three years and three months' duration [3] and one did the same after a partial remission of a few months' duration; one suffered a slight and temporary relapse after a complete remission of exactly two years' duration; one is a case of paresis sine paresi; seven represent satisfactory remission of from two to two and one-half years' standing, except in one instance, described elsewhere,[3] in which a depression of six months' duration succeeded an acute phase of hyperactivity, so that freedom from mental symptoms has now been present for only thirteen months. Among these seven are included two patients who, in addition to treatment with malaria, subsequently received twenty-four injections of tryparsamide, thirty-six injections of tryparsamide and twelve of neoarsphenamine, respectively, yet who have now reached only the status of the patients in the "modified" group; nevertheless, this almost minimal serologic result has not been inconsistent in either case with an excel-

lent clinical remission (of pretryparsamide onset) of nearly three years' duration. Included here also are three patients in whom the Wassermann reaction in the spinal fluid remains almost wholly unmodified at the end of two years, even though they have received subsequent treatment with tryparsamide; for in all five cases it is obvious that the influence of treatment with malaria alone on the Wassermann reaction of the spinal fluid would have been as slight as that of treatment with malaria and a certain amount of tryparsamide. There are, then, seven patients (of nineteen) in whom the persistence of a strongly positive Wassermann reaction in the spinal fluid for two years or longer has not been inconsistent with a maximum clinical therapeutic result of similar duration; on the other hand, among the same ninteen are also two cases of good and one of moderate remission in which a similar serologic situation was eventually attended by slight or partial clinical relapse.

TABLE 4.—*Wassermann Results in Relation to Clinical Outcome*

Wassermann Reaction	Moderate or No Mental Improvement	Good Remissions
Essentially unchanged	10*	9†
Modified	3	4
Much modified	6	5
Negative	4	6
	23	24

* Including one case of paresis sine paresi.
† Including two remissions with subsequent mental retrogression; including also two patients in whom only intensive treatment with tryparsamide served to modify slightly the Wassermann reaction.

In four of the seven cases in which patients show slight but definite modification in the strength of the spinal fluid Wassermann reaction there has been a remission of from two and a half to three and a half years' duration; in two cases, the patients are slightly improved and their condition is stationary as it is in one case in which the patient is unimproved. In five of the eleven cases in which there is considerable modification there have been remissions of from two and one-fourth to four years' duration; in two cases in which there is slight improvement the condition is stationary, as it is in four cases in which the patients are unimproved.

In six of the ten cases in which the Wassermann reaction of the spinal fluid has become negative there has been a remission of from two to three and three-fourth years' duration; in three cases the patients' condition remains clinically stationary with little if any mental improvement, while in one case in which there was no improvement, the patient died three years after treatment with malaria.

The only moderate degree of correlation existing between the therapeutic result achieved and the behavior of the spinal fluid Wassermann reaction which the foregoing data suggest appears in table 4. This table

shows that in this group of forty-seven cases about the same proportion of the patients treated experienced a satisfactory result as those that did not, regardless of the behavior (at least after from two to four years) of the spinal fluid Wassermann reaction. The reservation previously suggested applies here also, namely, that the survival of these patients for an average period of three years, especially since mental and physical retrogression are almost absent, would seem to signify the presence of some degree of therapeutic effect in nearly all these cases. Yet it must be borne in mind that the further lapse of time may show other changes; for it is conceivable, as two cases here described seem to indicate, that it is only in cases in which the Wasserman reaction is negative that extended remissions will be found, while in those in which the reaction of the spinal fluid is persistently more or less strongly positive, there may perhaps be an eventual relapse, although initially there is an equal therapeutic success.

SUMMARY

1. In sixty-five (72 per cent) of ninety cases of general paralysis in which there was a definite pleocytosis in the spinal fluid prior to treatment, an immediate reduction in the white cell count to normal (5 cells per cubic millimeter or less) or almost normal (from 6 to 10 cells per cubic millimeter) was exhibited following treatment with malaria. In ten additional cases a similar reduction required a month to manifest itself, in four three months, and in four, six months. In only seven cases was the pleocytosis unaffected by malaria treatment, in four cases it persisted until terminated by treatment with tryparsamide, which was begun after from seven to forty-three months; in three, by death after from three to eighteen months.

2. In twelve of sixteen patients an immediate and rather definite postmalarial reduction in the total protein of the spinal fluid occurred; but this tendency was more clearly in evidence at the end of one month, and especially evident at the end of three months. In a group of recently treated patients, the average total protein was 192 mg. per hundred cubic centimeters prior to treatment (twenty-two cases), 156 mg. immediately after treatment with malaria (sixteen cases), 124 mg. after one month (thirteen cases) and 91 mg. after three months (ten cases).

3. Of thirty-eight patients under observation during a posttreatment period of about two years, sixteen (or 42 per cent) now give a practically normal albumin reading of 50 mg. per hundred cubic centimeters or less (average, 42 mg.); eleven (or 29 per cent) give a "high normal" reading of from 50 to 75 mg. (average, 61 mg.), and eleven give a reading still definitely elevated (average 85 mg.), but only three of these are above 100 mg. A prognostic significance does not appear to be attached

to readings below 100 mg.; for, although the protein content of the spinal fluid in a number of mentally unimproved patients becomes normal, particularly after a sufficient lapse of time, in a few with remissions of considerable duration it continues to be from 80 to 100 mg. per hundred cubic centimeters.

4. Nineteen (or 40 per cent) of forty-seven patients, whose cases have been followed up for at least two years, have shown little if any modification in the strength of the Wassermann reaction in the spinal fluid; in seven there has been a slight though definite modification (to negative with 0.2 cc.); in eleven the reaction has become greatly modified (to negative with 0.5 cc.), and in ten it has become completely negative. The degree of modification which it is now possible to record in the majority of cases has required a period of from one to two and three-fourths years to make its appearance.

5. The behavior of the Wassermann reaction following malaria treatment seems to have little relation to the clinical outcome, at least as far as the present status of the latter is concerned. Cases of full remission make up about a similar proportion of each of the serologic groups here described; whereas a complete clinical remission of more than two years' duration has characterized nine of nineteen cases in which the Wassermann reaction has remained strongly positive, one of ten patients with a reaction which was ultimately negative has died, and in three the condition remains stationary and the patients have not improved.

6. Observations on the spinal fluid appear to be of prognostic significance only in a negative sense. A satisfactory response is not necessarily of favorable import; but the few cases in which reduction in the cell count does not take place with more or less promptitude or in which pleocytosis reappears, and those in which the total protein in the spinal fluid remains at or returns to a level in excess of 100 mg. per hundred cubic centimeters, seem to offer definite evidence of a minimum therapeutic result. The behavior of the Wassermann reaction in the spinal fluid does not seem to possess a decisive significance; but whether the cases with a more negative reaction will compare favorably with those with a less negative one regarding the ultimate duration of the therapeutic result achieved is a question to be answered in the future.

THE ELECTRICAL SKIN RESISTANCE

DIURNAL AND DAILY VARIATIONS IN PSYCHOPATHIC AND IN NORMAL PERSONS *

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Several years ago, in an endeavor to study experimentally the emotional reactivity of various psychopathic personalities, an investigation was made of the psychogalvanic reflex. In attempts to standardize the records so that the responses would be strictly comparable, however, great individual variations were encountered in the resistance offered by the body to the passage of a constant galvanic current. In order that this suggestion might be followed further, therefore, the electrical resistance was measured in each person to whom the psychogalvanic association test was given. When it was found that these incidental readings of resistance seemed to vary to a greater degree with different types of mental illness than did the psychogalvanic response, a detailed investigation of the electrical resistance of the human body was undertaken [1] in the hope that the significance of the more basic phenomenon of the resistance variations might be determined. In preliminary records, the lowest readings, from 20,000 to 40,000 ohms, were found in patients with early cases of schizophrenia and in patients with hyperthyroidism, and the highest readings, 1,000,000 ohms or more, in those in catatonic stupors. Interspersed between these two extremes were manic and depressive states and normal conditions. Despite the fact that persons of the manic and depressive types and normals were intermingled, these initial results suggested that there might be some fairly definite correlation between electrical resistance and mental state, and this suggestion constituted a point of departure for the present investigation.

Records were taken first of the resistance of the body at hourly intervals throughout the day, from the time of waking in the morning until bedtime, in order to determine whether, after all, the resistance did follow individual diurnal variations in mood and efficiency, as the preliminary work seemed to indicate, or whether it changed on a strictly physiologic basis in the same way that the body temperature curve

* From the Johns Hopkins University School of Medicine.

1. Richter, C. P.: The Significance of Changes in the Electrical Resistance of the Body During Sleep, Proc. Nat. Acad. of Sc. **12**:214, 1926; A Study of the Electrical Skin Resistance and the Psychogalvanic Reflex in a Case of Unilateral Sweating, Brain **50**:216, 1927; Physiological Factors Involved in the Electrical Resistance of the Body, to be published.

changes. The latter explanation is suggested by Waller[2] (1919), who found the electrical resistance of the body high in the forenoon, when the body temperature is normally low, lower in the middle of the day, when the body temperature is high, and high again in the evening, when the body temperature has begun to decrease. Waller limited his observations, however, to twenty-four-hour records for seven days on himself alone. Consequently, in his work, the large individual differences which may occur in diurnal resistance curves could not be realized. From the records of seventeen normal persons and thirty-three psychopathic patients, my associates and I have obtained a series of curves different from those of Waller.

In the next group of experiments, records were taken of the variations in resistance from day to day in a large group of normal persons and in patients, in an effort to determine whether the fluctuations in resistance are correlated with daily variations in any phase of the mental condition. In the normal subjects, variations in moods were reported by the introspective method and from mutual observation; in the patients, observations made by physicians and nurses in the wards had to suffice. In some instances, we were so fortunate as to obtain records on patients both during and after a definitely psychotic period, or during different phases of a prolonged psychosis, in which there could be no mistake as to marked changes in behavior and mental condition. From these daily readings, taken over a period of several months, it was possible to determine the degree of constancy in the large electrical differences observed between different types of persons and especially between the catatonic on the one hand and the tense paranoid schizophrenic patients on the other.

METHODS

In confirmation of the reports of previous investigations (Ebbecke,[3] 1921), we were able to demonstrate simply, and yet conclusively, that the electrical resistance offered by the body to the passage of an imperceptible constant galvanic current is localized practically entirely in the skin. We found that a minute puncture made through the skin with a hypodermic needle instantly reduces the body resistance from a level as high as 1,000,000 ohms or more to a few hundred ohms or zero. The resistance was measured with an Einthoven string galvanometer (Hindle model) according to a method already discussed in previous papers from this laboratory (Richter, 1926, 1927). The electrodes used, zinc disks with a kaolin paste, and the technic of preparing and attaching them have likewise been described. At the beginning of the present investigations, only two electrodes were employed, one attached to the palm and one to the back of the left hand, just as they were for the work on the psychogalvanic reflex. Later, however, in order

2. Waller, A. D.: Concerning Emotive Phenomena. Part II. Periodic Variations of Conductance of the Palm of the Human Hand, Proc. Roy. Soc. London **91**:17, 1919.

3. Ebbecke, U.: Die lokale galvanische Reaktion der Haut, Arch. f. d. ges. Physiol. **190**:230, 1921.

that the resistance of palm and back might be measured separately, two more electrodes were used, one in contact with the back of the right hand, and the other with the palm. Thus a current might pass not only directly through either hand, but also from the palm of one hand to the palm of the other, and from the back of one to the back of the other. These different connections were made quickly and easily from a switchboard bearing two double two-way switches. It may be mentioned in this connection that a far-reaching physiologic independence of the dorsal and palmar surfaces of the hands, so far as electrical resistance is concerned, has already been demonstrated in previous papers.

Since the present experiments were performed to study any differences which might arise in the resistance readings from a single person or group of persons, every possible precaution was taken to eliminate all variations caused by extraneous factors. Fresh kaolin paste was used for each record, and the skin was carefully cleaned before the experiment with alcohol and ether to remove any fat or oil present on the surface. Throughout the course of a diurnal record, the subject was instructed to wash the hands with lukewarm water only, without soap, since it seemed probable that either steaming or chilling the hands might greatly modify the resistance of the skin, and soap used by one and not by the other subjects might give rise to individual differences.

Because of the wide range of variations found in the preliminary studies, a large number of subjects were used in the subsequent work. The experiments on diurnal variations in skin resistance were performed in two series. In the first, the resistance offered to the passage of a current from the palm to the back of the left hand was measured in eleven normal and in twelve psychopathic persons. In the second series, the resistance offered to the passage of a current from palm to palm and from back to back was measured in eleven normal subjects and in twenty-four patients. Practically all types of psychoses were represented, but many of them were minor and the patients almost recovered.

In the experiments on daily resistance, records were taken on nine normal persons and thirty-three patients. Almost all types of major and minor psychoses were represented here, and in some cases records were obtained both at the height of the illness and for a period after a complete recovery.

RESULTS: DIURNAL VARIATIONS

SERIES 1.—In all of the first series of experiments, only three curves were found of the type described by Waller in which the resistance was high in the morning and evening and low at midday. A few of the records showed a constant low level from morning to night, and a few others, a constant high level, but most of the curves showed the early high resistance markedly decreased by noon, and maintained at the latter level throughout the remainder of the day. The various curves presented by normal subjects and patients are shown in charts 1 and 2.

Chart 1 shows the four different types of curves obtained from normals. In *A*, the resistance remains on an even low level throughout the day; in *B*, it begins slightly higher than in *A* but drops quickly within a few hours and remains low; in *C*, it is high at first, but here also it soon decreases rapidly; in *D*, it is highest in the morning, low at noon, and rising again in the early evening.

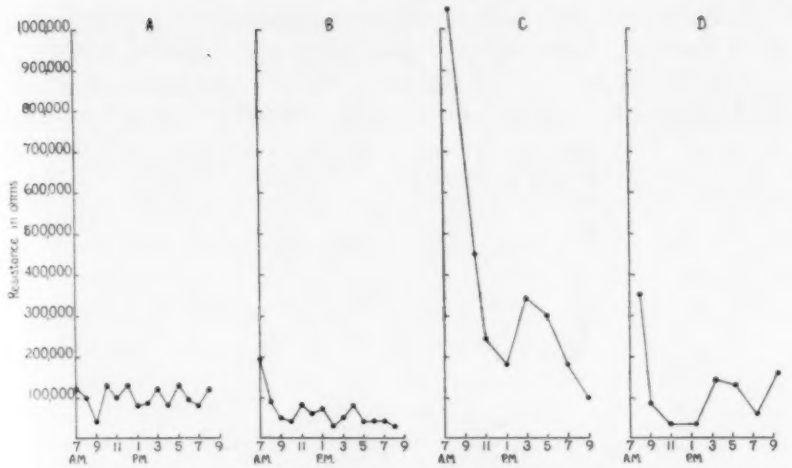


Chart 1.—Diurnal records of the resistance of the left hand, taken on four normal subjects, illustrating the four types presented by the eleven normal subjects studied and classified in table 1. *A* illustrates type 1 of table 1; *B*, type 2; *C*, type 3, and *D*, type 4.

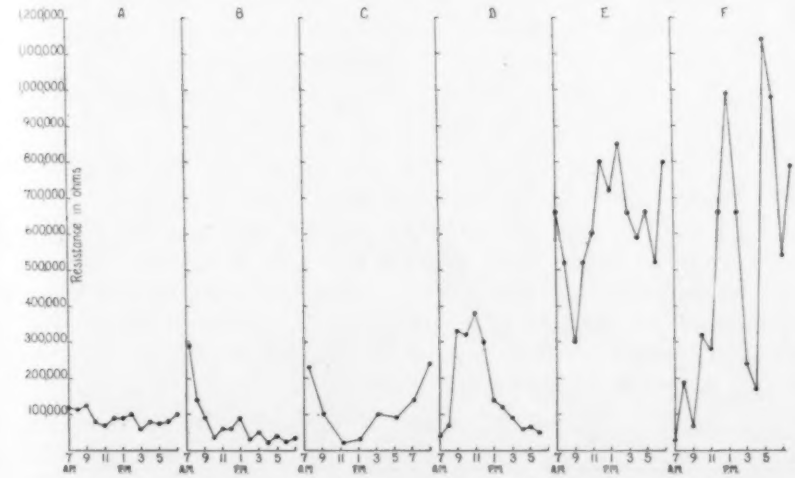


Chart 2.—Diurnal records of the resistance of the left hand, taken on six psychopathic patients, illustrating the six types presented by the twelve psychotic subjects studied and classified in table 1. *A* illustrates type 1 of table 1; *B*, type 2; *C*, type 4; *D*, type 5; *E*, type 6, and *F*, type 7.

From the results of these experiments summarized in table 1, it will be seen that five of the eleven normal persons showed the first type of curve, three the second, two the third and one the fourth type. The individual variations within each type were not great.

TABLE 1.—*Results of Records in First Series of Experiments*

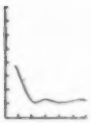
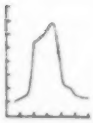
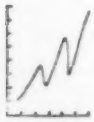
Type	Diurnal Curve	Normal Persons	Patients	Reaction Type of Patients
1		F. W. W. S. H. L. S. G. C. T.	H. C. H. G.	Schizophrenic Schizophrenic
2		A. H. L. K. S. K.	M. B. S. C. W. Z.	Schizophrenic Depression with schizophrenic features Reactive depression
3		M. I. R. G.		
4		G. W.	J. A. C. H.	Retarded depression with paranoid features Hypochondriacal depression with anxiety features
5			E. O'B. H. D. J. M.	Depression Hysterical reaction Depression with anxiety features and hallucinations
6			K. G.	Catatonic
7			A. F.	Stupor-catatonic ?

Chart 2 shows six of the seven different types of curves presented by the patients. In *A*, just as in the first curve in chart 1, the resistance is consistently low throughout the day; likewise the curve in *B* is similar to *B* in chart 1. Chart 2 *C* presents a good example of the type of curve

in chart 1 *D*, in which the resistance is high in the morning and the late evening and low at midday. In chart 2 *D*, *E* and *F*, new types of curves not found in normal persons are shown. In *D* the early low readings increase rapidly until a high level is reached. This high resistance persists throughout the morning and then decreases rapidly during the afternoon to the initial low level. In contrast to this record, the curve *E* is maintained at a constant high level throughout the entire day, and *F* shows marked fluctuations from one extreme to the other. The patients showing each of these different types are classified in table 1.

From the first series of experiments, the following data concerning the correlation of electrical skin resistance and mental state have evolved: 1. The resistance of the body, unlike the body temperature, does not conform to any average range of diurnal variation. Under normal circumstances, the twenty-four-hour body temperature curve takes essentially the same shape in all persons. The record of the skin resistance, on the other hand, varies widely throughout the diurnal period from subject to subject, normal and psychopathic alike. 2. The range of individual differences is great, as is shown by the fact that four types of curves were found in eleven normal persons and six types in twelve patients. 3. In the majority of cases, with the exception of the schizophrenic patients, the change from hour to hour is gradual, without any rapid fluctuations. 4. In normal as well as in psychopathic persons, the flat, low-level type of curve (chart 1 *A*) was accompanied by a tense, alert attitude throughout the day, whereas in the subjects whose resistance was high in the early morning and low in the evening (chart 1 *C*) the responses were retarded in the forenoon and did not reach an active, alert mental level until midday.

At this point, it occurred to us that a closer relationship might appear between skin resistance and mental condition if a distinction could be made between the resistance of the skin of the palm and of the back of the hand. It seemed probable that the palm, with its usual moist condition, might give readings different from those of the relatively dry back of the hand. In order that this analysis might be made, the method already described was developed, by which, with one electrode attached to the back and one to the palm of each hand, the current passed from the back of one hand to the back of the other, and from the palm of one to the palm of the other. With this addition, the same procedure used in the first series was applied in the second to a somewhat larger number of subjects.

SERIES 2.—When palmar and dorsal resistances were measured separately, it was found that in most subjects the shape of the diurnal curve, as well as the magnitude of the total resistance, depends almost entirely on the resistance of the skin of the backs of the hands, the palm-palm resistance usually remaining fairly constant and comparatively

much lower. That the difference between the contributions of these two areas is most striking in persons with catatonia will be seen later.

In this series, just as in the first, the psychopathic patients showed a range of individual differences much wider than was found in normal persons. In the various types of curves shown in charts 3, 4 and 5, the back-back readings are indicated by crosses and the palm-palm readings by circles.

Chart 3 presents five different types of diurnal resistance records on normal subjects. Chart 3 *A* shows a curve in which the back-back resistance is lower than the palm-palm, although that from palm to palm is unusually low. In *B* the back-back resistance begins high and gradually decreases, while the palm-palm curve remains on a flat low level throughout the entire day. In *C* the palmar and dorsal records are

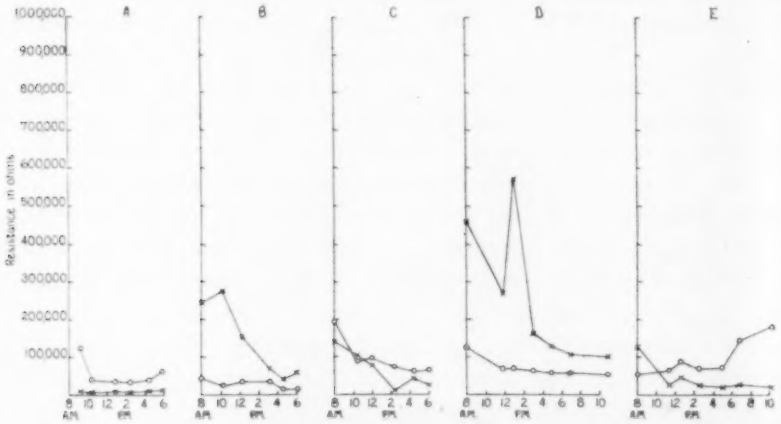


Chart 3.—Diurnal records of the palm-palm and back-back resistance of five normal persons, illustrating table 2. *A* illustrates type 1 *A*; *B*, type 2 *A*; *C*, type 2 *B*; *D*, type 3 *A*, and *E*, type 4 *B*. In this chart and in charts 4, 5 and 6, the back-back readings are represented by crosses and the palm-palm readings by circles.

approximately equal in the beginning and decrease at the same rate. The curve in *D* is similar to that in *B* except in so far as both back-back and palm-palm readings are much higher in *D* than in *B*. In *E* the back-back resistance starts high and decreases as usual, but the palm-palm curve increases steadily from hour to hour instead of remaining constant.

Records taken on patients are shown in charts 4 and 5. In chart 4 *A* which represents the record of a woman complaining of chronic "fatigue," the back-back and palm-palm records are both low, the back-back readings being practically zero. In *B*, the record of a convalescent psychasthenic patient, the dorsal resistance starts from a somewhat higher level and decreases during the day, while the palmar resistance is constant. The curve in *C*, the record of a patient with recurrent depressions,

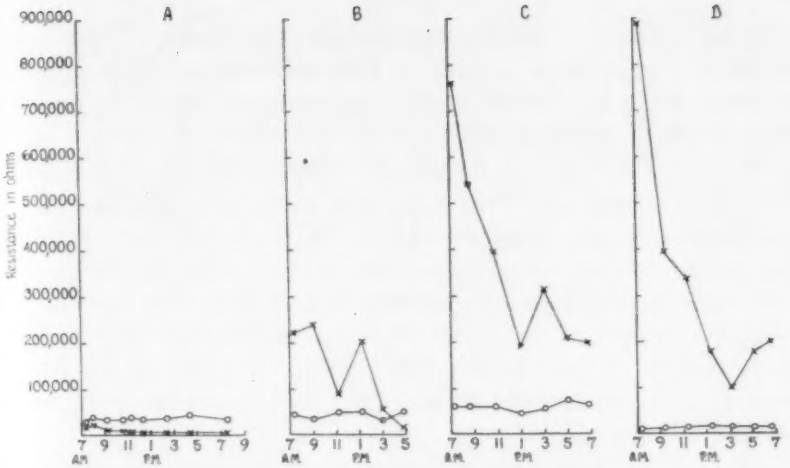


Chart 4.—Diurnal records of the palm-palm and back-back resistance of four psychopathic patients, illustrating the various types of table 2. *A* illustrates type 1 *A*; *B*, type 1 *A*; *C*, type 3 *A*, and *D*, type 3 *B*.

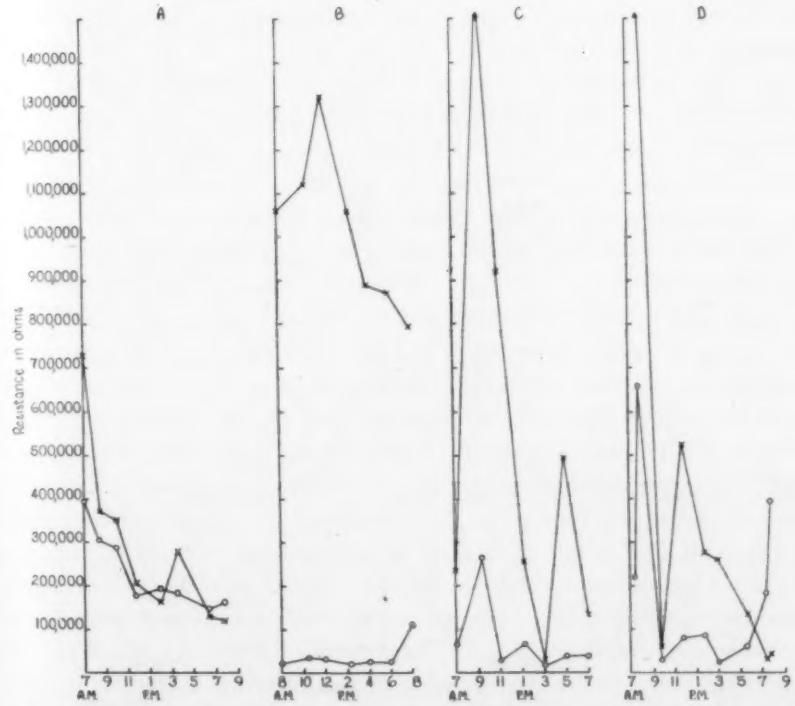


Chart 5.—Diurnal records of palm-palm and back-back resistance of five psychopathic subjects. *A* illustrates type 3 *C* of table 2; *B*, type 6; *C*, type 8, and *D*, type 9.

is similar to that in *B*, but the levels are consistently much higher. In *D*, the record of a catatonic patient, the back-back resistance starts high and decreases gradually throughout the day, while the palm-palm resistance remains low, at 10,000 ohms or less.

In chart 5 *A*, the record of a schizophrenic patient with depressive features, the back-back and palm-palm curves are both high in the morning and decrease gradually during the day, but even at the last two readings the level of both is higher than usual. Chart 5 *B*, the record of a catatonic patient, demonstrates the marked contrast between the back-back and palm-palm curves which is frequently encountered in such cases. Curves *C* and *D*, both from records of schizophrenic patients, show an extraordinary fluctuation from hour to hour in dorsal and palmar resistance alike.

Table 2, like table 1, is presented merely in an effort to summarize the diverse records obtained in the second series of experiments. The types of curve according to the total resistance on one hand are presented first, and comparison with table 1 shows that the seven types found in the earlier experiments appear here also, with two additional types (8 and 9) not found before. It can be seen that again the distribution of the normal subjects, with one exception, is limited to the first four configurations of the first series.

From this classification, as from table 1, it is evident that the diurnal skin resistance curve varies greatly in different types of persons, and further data become apparent concerning these variations: 1. The fluctuations throughout the day in both normal persons and patients arise largely from the skin of the backs of the hands which, with the exception of the porous areas (palmar and plantar), is probably representative for the skin of the rest of the body. The palm-palm resistance occasionally shows rather marked variations, and in catatonic patients it is maintained at a proportionately low level, but, on the whole, it remains relatively constant from person to person. 2. In normal subjects changes in resistance take place gradually, whereas in patients wide fluctuations often occur within an hour's interval. In schizophrenic patients of the passive type, for instance, the resistance rises and falls throughout the day from one extreme to the other. 3. It is significant to note in this connection that types 6, 7, 8 and 9 of table 2, as well as chart 3 *B* and *C*, included only schizophrenic and catatonic patients. In all the other groups, normal persons and patients of other reaction types alike were represented, with the exception of group 1 *B*. 4. The curve shown in that group was found in patients only: in the four who, of all those studied in the second series of experiments, complained chiefly of chronic fatigue; in a manic patient, and in an epileptic patient who had a grand mal seizure shortly after the last record was taken.

TABLE 2.—*Results of Records in Second Series of Experiments*

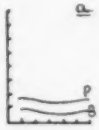
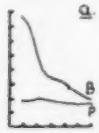
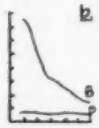
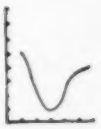
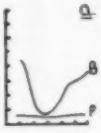
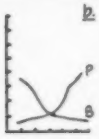
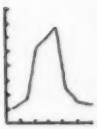
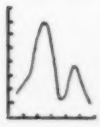
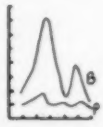
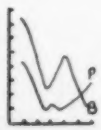
Type	Diurnal Curve: One Hand	Diurnal Curve: Back and Palm	Normal Persons	Patients	Reaction Type of Patients
1		a 	C. T. H. S.	L. N. E. U. E. A.	Agitated depression Manic depressive, manic phase Manic depressive
		b		R. S. A. B. F. M. K. W. F. Y. E. M.	Manic Fatigue, neurasthenia Fatigue, compulsive state Fatigue, depression and neurasthenia Fatigue, invalidism Epileptic
2		a	W. S. R. L. E. H.	J. B. J. H. C. D.	Epileptic Agitated depression Reactive depression
		b	G. W.		
3		a 	M. I. R. G.	D. C. M. A. E. O'B.	Encephalitic Psychasthenic depression Recurrent depression with anxiety features
		b 		F. H. C. S. K. G.	Catatonic Catatonic Catatonic
		c		M. T. J. W.	Schizophrenic with depressive features Schizophrenic with depressive features

TABLE 2.—*Results of Records in Second Series of Experiments—Continued*

Type	Diurnal Curve: One Hand	Diurnal Curve: Back and Palm	Normal Persons Patients	Reaction Type of Patients
4			a. B. B.	
			b. H. Z.	
5			E. K.	
6			W. S.	Catatonic
7			A. F.	Catatonic with schizophrenic features
8			E. J.	Schizophrenic
9			A. W.	Schizophrenic

To gain some idea of the extent to which the same type of diurnal curve persists in the same person, a few experiments were performed in which diurnal records were taken for four consecutive days on several psychopathic patients. Here again, as in all of the previous work, a great range of individual differences was encountered. A patient may show the same type of curve day after day, but the evidence, on the whole, suggests considerable variation in most cases. Furthermore, on the basis of the results obtained on the daily variations, one would expect the diurnal types to change from day to day in the same person.

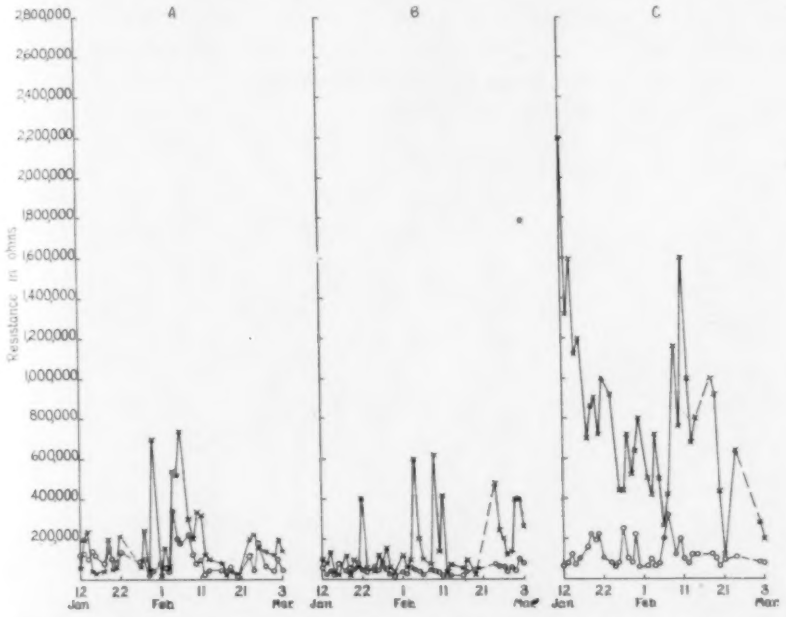


Chart 6.—Daily records on three normal subjects showing fluctuations from day to day in back-back and palm-palm resistance. The readings were taken between 9 and 10 o'clock each morning.

RESULTS: DAILY VARIATIONS

Resistance curves obtained daily over a long period of time from normal and psychopathic persons are presented in charts 6 and 7. Chart 6 shows records of resistance measured over a period of fifty days in three normal persons. In *A*, the back-back and palm-palm readings are low and nearly equal. In this subject, moreover, the palm-palm resistance fluctuated considerably from day to day and increased toward the middle of the experimental period after an illness in which there was a general nervous depression. In *B*, the palm-palm curve is remarkably constant, while the back-back resistance shows frequent fluctuations. Chart 6 *C* shows the back-back record much higher and more irregular,

while the palm-palm curve remains on a comparatively constant and much lower level. Of the nine normal persons studied, two showed the first, six the second, and one the third type of daily resistance curve. The individual variation was small compared to the wide variations found in patients.

In contrast to these normal curves, with regard to both the magnitude of the resistance and the degree of fluctuation, the three curves in chart 7 may be presented. In 7 *A*, the record of a schizophrenic patient of the tense, active type, both the palmar and the dorsal resistances are much lower than normal and show hardly any daily variation. The

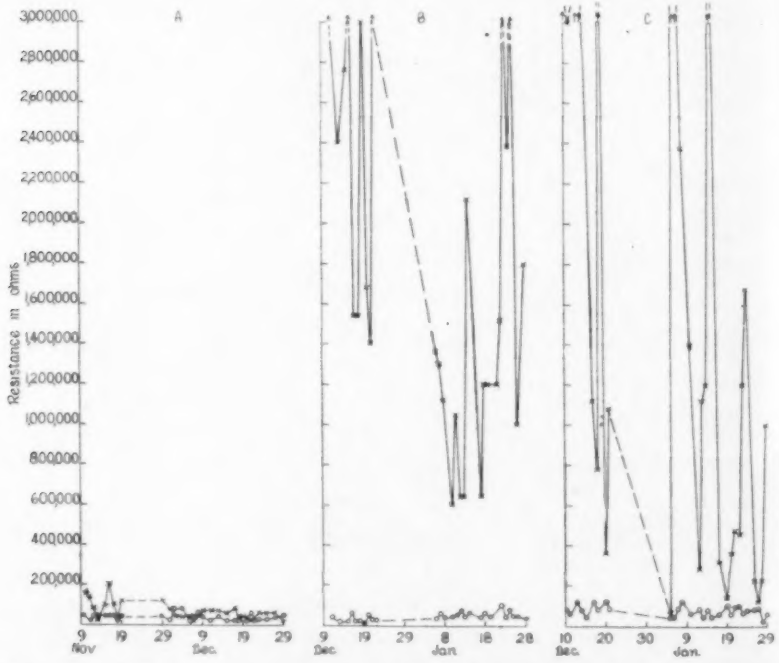


Chart 7.—Daily records on three psychopathic patients under the same conditions as described for chart 6.

curve in *B*, the record of a catatonic patient with a marked feeling of passivity, presents the other extreme. Here the back-back resistance is high, on some days more than 3,000,000 and never less than 600,000 ohms, whereas the palm-palm record is low, rarely exceeding 50,000 ohms. A somewhat similar curve is shown in *C*. In this record, obtained from a schizophrenic patient with depressive features, the back-back resistance shows extreme variations from less than 100,000 ohms on one day to more than 3,000,000 ohms on the next. The palm-palm resistance was slightly higher than usual in this patient but remained constant from day to day.

The records from both patients and normal persons show that the fluctuations in resistance are limited largely to the backs of the hands, the palm-palm resistance remaining comparatively constant. Furthermore, the large differences which define the various types are also localized chiefly in the back-back resistance. Of the thirty-three patients studied, twelve had catatonia or schizophrenia of the passive type. In all twelve the back-back resistance remained high while the palm-palm resistance was constantly low—in some, lower than the average. The patients at the other extreme, who showed a constant flat, low level of dorsal as well as of palmar resistance, had schizophrenia of the active or paranoid type. And, just as in the diurnal curves, the manic and depressive patients gave daily records which did not vary greatly from the normal. There was some tendency, however, for patients of the depressive type to show a higher and those of the manic type a lower resistance than normal.

TABLE 3.—*Records of Normal Persons*

Name	Number of Readings	Length of Time, Days	Back-Back Average	Palm-Palm Average	Ratio Back-Back to Palm-Palm
1. R. B.	50	107	721,300	105,900	6.81
2. A. B.	71	330	288,800	60,800	4.75
3. E. S.	35	50	123,400	31,000	3.98
4. F. R.	22	45	273,100	76,300	3.58
5. H. S.	78	107	194,000	54,700	3.55
6. E. K.	78	107	409,200	126,100	3.24
7. C. R.	121	427	228,000	72,400	3.15
8. G. W.	51	90	278,200	107,700	2.58
9. L. S.	45	98	96,800	59,000	1.64
Average			290,310	77,100	3.70

These differences are brought out clearly by the individual averages of all readings taken on each patient and normal person. The normal averages are shown in table 3. Attention may be called to the numerous readings taken on each subject; in one instance, 121 readings were taken over a period of 427 days. The table shows that the average back-back resistance for the nine subjects was 290,310 ohms, and the palm-palm resistance 77,100 ohms, the back-back readings varying from 96,800 to 721,300 ohms, and the palm-palm from 31,000 to 126,000 ohms. On the basis of these readings, also, it would appear that the individual variations in normal persons are large. When, however, the ratio of the back-back to palm-palm resistances is considered, a striking fact comes to light. Here the average ratio for the group is 3.70; five subjects show ratios deviating little, two others are slightly above, and the other two are slightly below this average (the highest, 6.81; the lowest, 1.64). The significance of this ratio can be seen clearly when the averages for the different types of patients are considered.

The averages for the thirty-three patients are given in table 4. The patients are listed according to the back-back: palm-palm ratio, which varies from 44.93 to 1.13. The first twelve patients show an average of from 15.25 to 44.93, which is much above the normal 3.70. Of these twelve patients, eleven had catatonia or schizophrenia with a marked feeling of passivity; the other was a postencephalitic patient. This list includes every catatonic or schizophrenic patient with feelings of passivity in the entire group except one, whose average was 10.29,

TABLE 4.—*Records of Patients*

Name	Number of Readings	Length of Time, Days	Back-Back	Palm-Palm	Ratio Back-Back to Palm-Palm	Reaction, Type
1. J. B.....	29	50	1,874,480	41,720	44.93	Catatonic
2. D. L.....	16	21	1,291,120	32,810	39.35	Catatonic
3. M. C.....	43	105	698,880	22,670	30.82	Schizophrenic
4. T. M.....	44	240	2,088,720	76,250	27.39	Catatonic, schizophrenic
5. J. C.....	35	47	1,055,940	40,280	26.21	Schizophrenic
6. C. B.....	21	43	1,028,450	42,880	23.98	Catatonic
7. E. S.....	10	10	2,512,800	106,000	23.70	Catatonic, schizophrenic
8. D. C.....	5	16	944,000	41,000	23.00	Postencephalitic
9. C. S.....	13	70	452,300	20,760	21.78	Catatonic
10. M. R.....	54	80	1,134,290	65,640	17.29	Catatonic, schizophrenic
11. A. K.....	22	104	1,960,540	115,220	17.06	Catatonic
12. T. H.....	113	480	292,950	19,200	15.25	Catatonic, schizophrenic
13. G. H.....	27	43	1,322,810	103,510	12.78	Narcoleptic
14. F. T.....	5	15	384,000	34,000	11.30	Manic ?
15. E. S.....	9	15	401,110	36,110	11.10	Depression
16. M. L.....	30	35	226,500	22,000	10.29	Catatonic stupor
17. J. B.....	13	36	485,380	48,070	10.09	Senile depression
18. R. D.....	78	360	519,970	65,250	7.96	Depressive stupor
19. J. W.....	9	10	496,000	63,330	7.83	Schizophrenic
20. R. R.....	10	27	638,500	87,500	7.29	Schizophrenic
21. H. O.....	20	48	812,250	123,250	6.59	Manic
22. J. L.....	32	100	296,720	48,120	6.16	Manic
23. Z. R.....	38	51	613,550	102,230	6.00	Hysteric
24. L. S.....	24	42	508,330	101,870	4.99	Depression
25. M. V. E...	44	102	307,160	78,750	4.66	Schizophrenic
26. A. S.....	123	285	374,100	128,130	2.92	Narcoleptic
27. M. T.....	20	93	388,750	162,750	2.38	Schizophrenic
28. E. B.....	17	39	197,060	88,820	2.22	Anxiety depression
29. G. S.....	16	28	148,120	72,810	2.03	Narcoleptic
30. E. McL...	24	55	73,120	40,000	1.82	Manic
31. E. S.....	16	32	689,000	418,750	1.64	Narcoleptic
32. R. L.....	31	67	78,000	48,220	1.62	Schizophrenic
33. L. A.....	29	70	40,860	36,200	1.13	Schizophrenic
Average.....			739,450	76,790	13.13	

still well above the average. At the other extreme were two schizophrenic patients of the active or paranoid type, whose averages were 1.13 and 1.62. In this table it can be seen that although the rank of the patient generally seems to follow the back-back resistance, there are a few exceptions. In the twelfth patient, for instance, the back-back resistance was 292,950 ohms, far below that of most of the other catatonic patients, but in this patient the palm-palm resistance was only 19,200 ohms, so that the ratio was as high as that of the others. Here again the records of the manic, depressive, narcoleptic and hysterical patients fell between the two extremes, deviating only slightly above and below the normal.

Thus far the efforts to correlate mental changes in normal subjects with daily fluctuations in resistance have been only partially successful, since it has been found impossible for the subject to describe his mood from day to day with even a fair degree of accuracy unless the mental changes have been sharply defined. If the moods fluctuate slowly, he tends to lose perspective on his attitude, and introspection becomes valueless. It may be noted, however, that periods of sullen hopelessness are associated with a fairly high back-back resistance and a low palm-palm resistance, similar to records obtained in catatonic patients. On the other hand, as might be expected, periods of marked tenseness

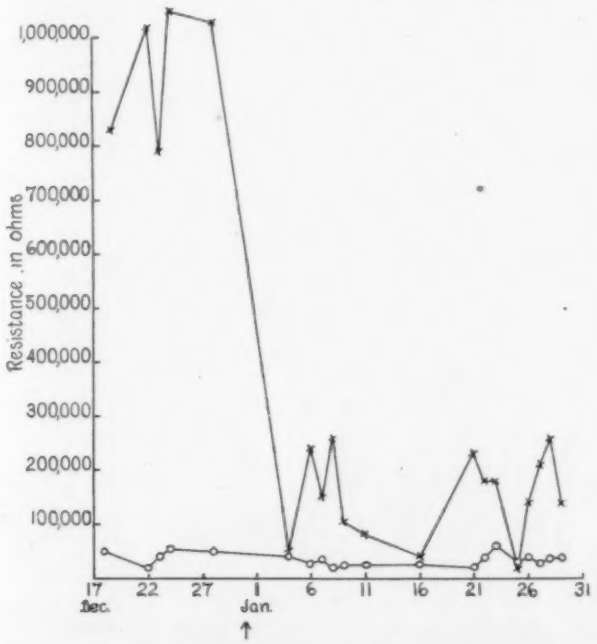


Chart 8.—Record of daily resistance of a postencephalitic patient, showing high back-back resistance during the first two weeks, and marked decrease thereafter, associated with sudden change in behavior. The palm-palm record maintains a constant low level. In this chart and in chart 9, the arrow indicates the day on which the change occurred; the crosses indicate back-back readings, and the circles, palm-palm readings.

and nervousness are associated with low back-back resistance. And in subjects who felt definitely depressed, the palm-palm resistance rose to a much higher level than usual.

In patients, significance was not attached to introspective accounts, but reliance was placed solely on clinical observations. Daily records were obtained on a number of patients who showed striking changes in behavior during their stay at the hospital. The record of a post-

encephalitic patient is shown in chart 8. For the first two weeks in the ward, the boy was unruly, irritable, sullen and combative. He was also careless in his habits and in the condition and arrangement of his clothing. During this time the back-back resistance maintained a level near 900,000 ohms. Then suddenly, almost over night, he emerged from this condition and became friendly, natural and neat. With this striking change in behavior, the resistance dropped suddenly and

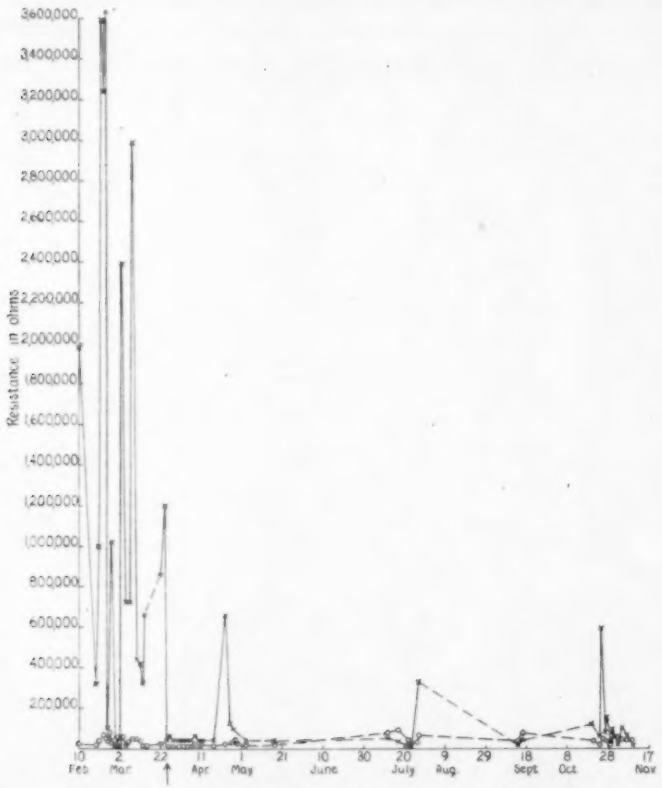


Chart 9.—Record of daily resistance of a catatonic schizophrenic patient showing change in level of back-back resistance with change in behavior and mental condition (indicated by arrow). The palm-palm resistance maintained a constant low level throughout the experiment.

remained at a much lower level until the patient was discharged several weeks later.

Another patient showing marked fluctuations in conduct was of the schizophrenic reaction type with catatonic features. The record of his resistance is presented in chart 9. For a long time, the patient was in a semistuporous condition, mute, resistive and occasionally cataleptic. Throughout this period the back-back resistance, although high, fluctu-

ated considerably. Then suddenly, within a few days, he showed a marked change in behavior, becoming active and talkative, and continued in this condition until he left the clinic several months later. Just preceding the change, the resistance dropped and, except for a few days, persisted at a permanent low level.

In still another patient, who suffered from periodic outbursts of rage, there were also striking changes in electrical resistance coincident with the changes in behavior. Normally this patient, a boy aged 17, was friendly, did well at school and was well liked by his companions. During the attacks, however, the face took on a sullen, angry expression.

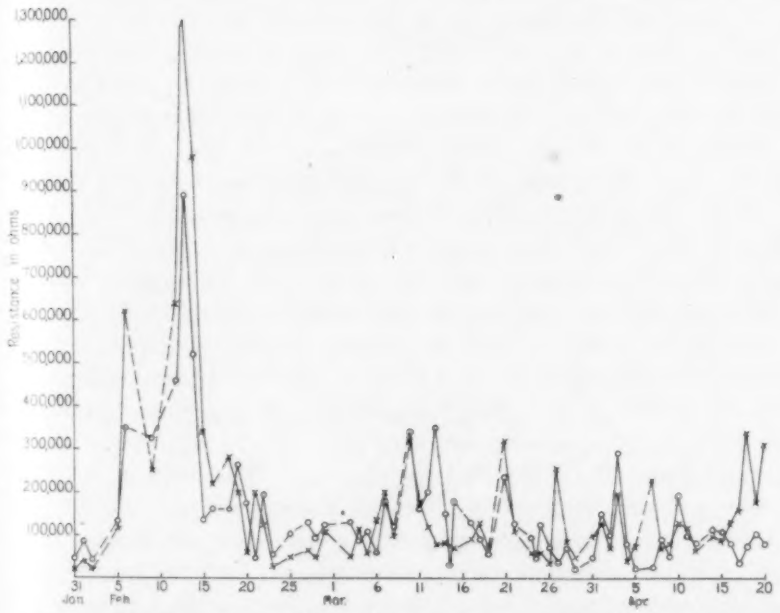


Chart 10.—Record of daily resistance of a patient suffering from periodic outbursts of rage. The back-back readings are indicated by crosses; the palm-palm readings, by circles. The high peak, with the back-back resistance at 1,900,000 ohms and the palm-palm readings at 900,000 ohms, was associated with one of the attacks of rage.

and he became combative and sometimes suicidal. For a few days just preceding each attack that he experienced while under observation, the resistance dropped almost to zero; during the outburst the back-back and palm-palm readings both rose very high. The record in chart 10 shows the changes in resistance associated with the last attack, which started on January 31 and continued for several weeks. During this time, both the back-back and the palm-palm resistance remained high. Then the attack gradually subsided, and the boy's behavior appeared normal for a few days before he began to show signs of tenseness and

strain. By February 23, the resistance had dropped to a low level and a new attack was expected. From that time, for the three weeks following, he received phenobarbital daily. An attack did not occur and he gradually adjusted himself to what seemed to be his normal behavior level. Simultaneously, the skin resistance presented a more normal picture and was maintained at a relatively constant level up to his dismissal from the clinic on April 20.

These three records are the most outstanding, but similar changes of daily resistance with variations in conduct have been demonstrated by observations on a number of other patients whose behavior and attitude fluctuated from week to week during their stay in the hospital.

COMMENT

It can be seen from these results that skin resistance is subject to much wider fluctuations than almost any of the other physiologic functions of the body. Those most commonly known, body temperature, pulse rate, respiration, basal metabolic rate, etc., all remain extraordinarily constant from day to day and from person to person, except under pathologic conditions. Any changes which do occur in these functions are normally so transient and so quickly brought into equilibrium by various compensating mechanisms that individual differences which arise are usually small. For this reason, efforts to correlate these factors with mental and emotional conditions have not proved successful.

Skin resistance, on the contrary, shows chronic individual differences and, at the same time, an extraordinary sensitivity to alterations in the emotional and mental condition of the subject. Thus, both the diurnal and daily resistance curves of psychopathic patients deviate considerably from similar curves obtained from normal subjects. It is especially interesting to note that these large differences in resistance are present in many instances when, by casual observation, peculiarities in behavior cannot be detected. In some catatonic patients, for example, the skin resistance is often extraordinarily high, even when casual conversation with the patient fails to reveal any abnormality; and more prolonged clinical observation of the case usually confirms the diagnoses based on the records of electrical resistance. The question arises now as to the significance of individual differences in resistance. To what extent can conclusions be drawn concerning the mental state of the subject from records of his skin resistance?

In previous papers, it has been shown that the resistance of the palm of the hand is chiefly dependent on the activity of the sweat glands, and is controlled by nervous impulses partly from sympathetic and partly from somatic nerves. The back-back resistance, however, is dependent on the epithelial cells and is largely, if not entirely, free from nervous control. Both dorsal and palmar resistance were shown to be

influenced by the heat-regulating mechanism of the body. The palmar resistance decreases or increases following the activity of the sweat glands as they dissipate more or less heat, while the dorsal resistance seems to follow the activity of the epithelial cells as they give off heat through the evaporation of moisture in the form of insensible perspiration. Furthermore, in keeping with the current theory that ordinary demands for control of temperature are met by insensible perspiration and only emergency or pathologic demands are met by increased sweating, it has been pointed out that the back-back resistance shows large fluctuations while the palm-palm record remains relatively constant. This theory would seem to be confirmed in the present work by records taken on a much larger group of subjects over a longer period of time.

The back-back resistance, which seems to be representative of the resistance of all other nonporous areas of skin, varies, we believe, with the amount of heat liberated by the muscles under varying degrees of tension. The heat produced stimulates the epithelial cells, increasing their permeability, and more moisture is given off. In tense, strained subjects one would expect to find a high permeability of the dorsal surfaces and in persons free from strain, a low permeability. That such a condition is found has been amply demonstrated by the experiments reported.

Variations in the palm-palm resistance are associated with changes in the central nervous system, rather than with changes in the muscles. In the papers mentioned it has been demonstrated that the palmar resistance shows a large increase during sleep, following nerve section and severe shock, and just preceding and following death. In all these conditions the impulses reaching the skin are diminished either through a depression of the central nervous system or through actual interruption of the nerve pathways. In the present series of experiments, it has been found that a high palm-palm resistance over a prolonged period of time is apt to be associated with a depressed mental condition, while high individual palm-palm readings are associated with a feeling of sleepiness. It is interesting to note in this connection that the palm-palm resistance has been found at a chronic high level in some of our narcoleptic patients, even when they were not having a sleeping attack; during the attacks the resistance showed a marked additional increase. The results of the experiments on these patients will be presented in detail in another paper.

SUMMARY

1. The electrical skin resistance was measured in twenty-six normal persons and in sixty-six psychopathic patients. In two series of experiments, readings of skin resistance were taken at hourly intervals throughout the day to determine the differences in the diurnal curves of normal subjects and patients. In another series, records were taken once each

day over long periods of time to observe daily variations in normals and patients.

2. Throughout the work the normal subjects gave records which remained fairly constant, not showing any wide individual differences. In marked contrast, many of the patients presented records with large individual differences and at the same time great variation from the normal. These patients were all either catatonic or schizophrenic. The schizophrenic patients with marked feelings of passivity deviated to one extreme; those of the active or paranoid reaction type deviated to the other.

3. The records from manic, depressive and hysteric patients deviated slightly, but were still within the limits of normal variation. A group of patients whose chief complaint was chronic "fatigue" also gave records which were distinctive, and it is interesting to note that all of these patients consistently presented the same type of record.

4. The physiologic origin of these differences in readings of resistance in normal persons and in different types of patients was discussed. It was shown that differences in emotional and mental condition can be measured more satisfactorily by skin resistance than by many of the other physiologic responses, such as blood pressure, basal metabolic rate and body temperature, because any differences in the latter are always quickly compensated and brought back to a normal level.

5. This method has one important advantage in that readings can be taken easily and quickly and can be repeated at frequent intervals.

TUMORS OF THE POSTERIOR CRANIAL FOSSA

HOMOLATERAL AND CONTRALATERAL PYRAMIDAL TRACT SIGNS *

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In unilateral expanding lesions above the tentorium, increase in the tendon reflexes is usually greater on the side of the body opposite to that of the lesion; this is readily explained.

In infratentorial new growths, there are many variations in the tendon reflexes on the two sides; in some instances, the reflexes are unchanged; in others, all tendon reflexes are diminished; in some patients, there is a bilateral and equal increase; in others, there is a homolateral or contralateral hyperreflexia. No special studies of the disturbances of the pyramidal tract and few statements concerning the possible significance of the alterations in the tendon reflexes in new growths limited entirely or mainly to one side of the posterior cranial fossa are to be found in the literature.

The records of about 150 patients with subtentorial expanding lesions have been reviewed, but the histories in only fifty cases have been used for this study. The remainder were discarded because either the data were incomplete or other lesions were discovered at autopsy, or because operation or postmortem examination showed that the tumor involved both cerebellar lobes or was primarily a midline growth in or near the vermis. In the fifty histories that form the basis for this paper, the location and nature of the tumor were verified either by operation and pathologic examination of the tissue removed or by autopsy—except in a number of instances of presumably gliomatous cysts of one cerebellar lobe in which tissue for microscopic study had not been removed. In twenty-four of the fifty cases the tumors were lateral recess growths—chiefly acoustic neuromas—and in twenty-six the tumors—most often cystic gliomas—were in one cerebellar lobe. From this material an attempt has been made to answer the four following questions.

1. What is the frequency of homolateral and contralateral increase of tendon reflexes? The evidences of involvement of the pyramidal tract in cases of posterior fossa tumors are rarely so marked as to be considered prominent symptoms. In my series of cases, the objective evidence of disturbances of the pyramidal pathways varied from a slight to a marked increase in many of the tendon reflexes with or without ankle clonus. In some of the patients, the reflexes were hyperactive only

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on one side, while in others, the hyperreflexia was bilateral but was definitely greater on one side than on the other. Six patients had more or less well marked weakness of the limbs on one side of the body; in five of them, the loss of power affected the limbs of the same side as that of the lesion.

Extension of the large toe on irritation of the sole of the foot was noted in six patients—in five with a glioma in the cerebellar lobe and in one with a tumor in the cerebellopontile angle. In four patients, the Babinski sign was unilateral and in two bilateral. In his monograph on acoustic nerve tumors, Cushing found a Babinski reflex in two of thirty patients.

The alterations in the tendon reflexes in cases of infratentorial tumors are given in the accompanying table:

Changes in Tendon Reflexes in Fifty Infratentorial Tumors

	Number of Cases	Percentage Unilateral Increase	Percentage Totals	
Homolateral increase	27	73	54	74
Contralateral increase	10	27	20	
Bilateral or no increase	13	..	26	
Total number of cases	50			
Lateral Recess Growths				
Homolateral increase	16	84	67	79
Contralateral increase	3	16	12	
Bilateral or no increase	5	..	21	
Total number of cases	24			
Intracerebellar Tumors				
Homolateral increase	11	61	42	69
Contralateral increase	7	39	27	
Bilateral or no increase	8	..	31	
Total number of cases	26			

2. Is there any discoverable relation between the size and location of the growth and the occurrence of the changes in the tendon reflexes, and is there any parallelism between the degree of ventricular distention, of papilledema and of involvement of the cranial nerves, on the one hand, and of disturbance of the pyramidal tract on the other?

As far as could be determined in my small series, a distinct relation was not present between the amount of involvement of cranial nerves and the evidence of a condition in the pyramidal tracts. Disregarding the loss of hearing in fibroblastomas of the acoustic nerve, in which the new growth begins in the sheath of that nerve, and the secondary affection of the seventh cranial nerve of the same side, a parallelism between the evidence of disturbance of these nerves and the homolateral or contra-

lateral changes in the tendon reflexes was not found. Furthermore, as was to be expected, the amount of abducens palsy did not bear any relation to the signs in the pyramidal tract. The same was true regarding involvement of the homolateral trigeminus. Finally, there was no evidence that the disturbances of the pyramidal tract were more frequent in the patients in whom the hypoglossal nerve of the same side had been affected.

There was no relationship between the size of the new growth and the changes in the tendon reflexes, although in large tumors with marked pontile and medullary symptoms, all tendon reflexes were often diminished. Small tumors, however, often caused as marked hypereflexia as did large ones, but it is my impression that small intracerebellar growths less often caused changes in the reflexes than did tumors of a similar size of the auditory nerve. Nor was it possible to find a relationship between the degree of papilledema and the amount of ventricular distention on the one hand and the increase of the tendon reflexes on the other. While a rise in intracranial pressure from obstructive hydrocephalus should be followed by an increase in the signs of interference with the pyramidal pathways, marked disturbances in muscle tone often interfere with or prevent changes in the tendon reflexes.

Tumors in a lateral recess or in a cerebellar lobe vary in their location, in their relations to the surrounding structures and in the amount of dislocation and deformation which they produce in the pons and medulla. In most of the patients of this series, the anatomic observations were based on operative records, and the data concerning the exact relations of the tumor were necessarily meager. The cases in which postmortem studies could be made were few; therefore conclusions concerning the relationship between the location of the tumor and the occurrence of the changes in the tendon reflexes could not be drawn. There must, however, be a relationship between these factors and signs of interference in the motor pathways.

3. Is a satisfactory explanation for the alteration in tendon reflexes to be found in local or general pressure conditions within the cranial cavity? In the search for an explanation for the occurrence of homolateral and of contralateral changes in the tendon reflexes, four locations of pressure on the pyramidal tracts may be considered: (*a*) in the cerebral hemispheres, (*b*) in the cerebral peduncles, (*c*) in the pons and (*d*) in the medulla.

Elsberg and Silbert have recently called attention to the fact that in tumors of the unilateral posterior fossa, especially those in the cerebellopontile angle with obstructive hydrocephalus, the opposite lateral ventricle is often more dilated than the homolateral one. Such an unequal dilatation of the two lateral ventricles might produce a hyperreflexia more marked on the same side as the lesion of the posterior

fossa. The difference between the size of the two lateral ventricles is, however, slight, and it is unlikely that this difference in size is a factor of any importance.

Besides the amount of ventricular dilatation, the degree of intraventricular pressure might be a factor. There may be a high intraventricular pressure without marked distention, and in such a case there might be a difference between the pressure in each lateral ventricle and therefore a greater amount of pressure through the thalamus on the internal capsule of one hemisphere. This difference between the two sides, if it does exist, is too small to have any significance.

While pressure on the cerebral peduncle of the same side with resulting disturbances of the pyramidal tract by a neoplasm in the anterior part of the lateral recess or attached to the under surface of the tentorium or in a cerebellar lobe is possible, it has not been demonstrated. Dislocation of the brain stem with pressure of the contralateral crus against the free margin of the tentorium might be considered as an explanation of the homolateral increase in the tendon reflexes. To bring about such a condition, the brain stem would have to be dislocated toward the other side, or the free edge of the tentorium would have to be drawn over toward the side of the expanding lesion—a condition which would be unusual.

Direct pressure on the side of the pons with the formation of a more or less well marked depression in this part of the brain and dislocation of the pons toward the opposite side is frequent in lateral recess growths. It is more rare in expanding lesions within a cerebellar lobe, unless they are large. One might expect that, in the former, contralateral signs in the pyramidal tract would be of frequent occurrence, but in reality an increase in tendon reflexes on the same side as the new growth is more often observed. The cisterna pontis acts as a fluid pad which protects the ventral and ventrolateral surfaces of the pons from the bone, and the pressure of a neoplasm on any surface of a cerebellar lobe or within its substance would have to be great to overcome the protection of this fluid buffer. It is doubtful, therefore, whether transmitted pressure or "contrecoup" will explain homolateral disturbances of the pyramidal tract caused by pontile involvement.

The ventral surface of the medulla is only partly covered by the downward extension of the cisterna pontis and is in rather close contact with the basi-occipital bone. The pyramids fit fairly snugly into the concave surface of the bone, and in many cases the ventrolateral sulci lie against the more or less distinct edge of the concave surface.

A growth in the cerebellopontile angle, on the inferior surface of the tentorium or in the lateral portion of a cerebellar lobe, may press directly on the lateral surface of the medulla and cause a more or less well marked depression in it. Pressure on the homolateral pyramid can

thus be easily explained. Often, also, the medulla is dislocated toward the other side, and the contralateral pyramid is pressed against the bone. One or both of these physical alterations may well explain changes in the tendon reflexes, more marked in the limbs of the same or of the opposite side of the body.

It is, however, possible that the "contrecoup" pressure may be exerted above, at the level of, or below, the pyramidal decussation. As a result, the degree of disturbance in the motor pathways might vary with the difference in the amount of pressure on one side. Whether a certain amount of foraminal herniation of the cerebellum may contribute to the pressure on the medulla and therefore on the pyramids or the decussating fibers is an open question, but it seems possible that the resistance of the margin of the foramen magnum may add another factor which should be considered in this relation.

To summarize: The most likely region in which the pyramidal tracts are involved is the medulla, and the greater pressure on the contralateral pyramid by "contrecoup" must occur more often than one expects. In growths in a lateral recess, in which the tumor is more or less firmly fixed to the dura, the tumor is often "capped" by an "arachnoid cyst" which is apt to act as a buffer and to protect to a certain extent the pyramid of the same side from a direct and continuous pressure, while the contralateral pyramid is pressed against the hard, unyielding bone. The mechanism is similar to that which occurs in some tumors of the spinal cord that are adherent to the dura and that cause more marked contralateral motor disturbances. This will explain also why homolateral changes in the tendon reflexes are less frequent in intrinsic expanding cerebellar disease (42 per cent of the total of intracerebellar tumors and 61 per cent of intracerebellar tumors with more marked unilateral changes in the tendon reflexes) than those in the extracerebellar lateral recess and tentorial growths (67 per cent of all of the extracerebellar tumors and 84 per cent of the extracerebellar tumors with unilateral hyperreflexia).

4. Of what value are changes in the tendon reflexes for the diagnosis of subtentorial expanding lesions? The relative frequency of homolateral changes in the tendon reflexes in tumors of the posterior fossa should be of value in some cases in which the signs of a tumor in the cerebellar lobe or in the cerebellopontile angle are vague and indefinite. For example, in the following case, it might have led to a better explanation of the symptoms presented by the patient.

A middle aged woman was admitted to the Fourth Division of the New York Neurological Institute. She had complained for some time of marked and persistent formed hallucinations of vision, loss of vision and headache. On examination she was found to have an increase in the tendon reflexes on the left side of the body, slight left facial weakness, and diminution in the hearing

of the left ear, which she said had come on following a cold. The patient had never had tinnitus, and there was no nystagmus or diminution in the sensation of the cornea on either side. There appeared to be slight weakness of the left upper and lower limbs; a slight and questionable unsteadiness in the movements of the left upper extremity was believed to be the result of the motor weakness. On account of the predominant hallucinations of vision and the contralateral motor signs, a tumor of the right temporal lobe was suspected. The patient died after an exploratory operation, and autopsy revealed a left acoustic neuroma.

If the relative frequency of homolateral disturbances of the pyramidal tract in tumors in the cerebellopontile angle had been realized, more attention might have been directed to the possibility that the patient had a left angle new growth.

SUMMARY AND CONCLUSIONS

Fifty cases of unilateral tumors of the posterior fossa were studied. Seventy-four per cent of these had more marked signs of the pyramidal tract on one side of the body. In 73 per cent (or 54 per cent of all the cases) of the cases in which there were relative unilateral changes there was a relative increase in tendon reflexes on the same side as the expanding lesion. In twenty-four patients, the neoplasm was in the cerebellopontile angle, and in 79 per cent of these the reflexes were more active on one side of the body; in 84 per cent, the hyperreflexia was greater on the same side as the lesion. In twenty-six patients the tumor was within the substance of one cerebellar lobe, and in 69 per cent of these, the reflexes were more active on one side of the body. In 61 per cent of these patients, the hyperreflexia was greater on the same side as the lesion.

In obscure intracranial expanding disease, especially when there is a question whether the growth is supratentorial or infratentorial, the changes in the tendon reflexes on the two sides of the body may assume considerable importance. This is especially true when there is a difference between the disturbances of the pyramidal tract on the two sides of the body, for a relative increase in tendon reflexes on one side of the body may and often does occur with infratentorial tumors of the same side. Furthermore, because homolateral increase in tendon reflexes is considerably more frequent in lateral recess than in intracerebellar growths, the occurrence of a relative hyperreflexia on the same side as the cranial nerve and "cerebellar" disturbances may be of aid in the differentiation between extracerebellar and intracerebellar disease.

SYMPATHETIC IRRITATION IN A CASE OF ACTINOMYCOSIS

REPORT OF A CASE *

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In 1727, Petit [1] first observed the influence of the cervical sympathetic nerve on the eye. Since that time, the effects of paralysis or irritation of the sympathetic nerves have commanded much study, particularly in the interval following the experiments of Claude Bernard, and during the World War. Attention has been focused on the cervical sympathetic system, mainly because the ocular effects of changes in the cervical sympathetic nerves are so striking and obvious. The consequences of alterations of the nerves or ganglia in other parts of the sympathetic system have received much less general attention, though they must be fully as important. A number of cases are on record in which injuries of the brain, cord or peripheral nerve trunks have occurred, with various sequelae, which were probably due to sympathetic involvement. Chief among these are the interesting observations of André-Thomas,[2] who has studied such cases on an exhaustive scale, stressing the changes that occur in the pilomotor reflex.

As far as we have been able to learn, however, there are only two reports recorded in which the symptoms resulting from damage to the thoracic or lumbar sympathetic system, uncomplicated by involvement of the sensory or motor nerves, have been studied. In one of these cases, a patient of André-Thomas,[3] had an aneurysm of the thoracic aorta, which impinged on the first, second and third thoracic sympathetic ganglia, causing signs of paralysis of the sympathetic nerves in that distribution. There were no changes referable to any spinal nerves. The entire left upper extremity and the left side of the face and chest showed absence of the pilomotor reflex; sweating was decreased on the left side of the face and absent from the left upper extremity and the left side of the chest. The examiner's finger, drawn across the front of the chest, elicited a much greater reaction on the left than on the right side. Thermal changes were marked; in an ordinary room, the left hand was usually warmer than the right; after immersion in ice water, the left

* From the Mount Sinai Hospital.

1. Petit: Histoire de l'Acad. royale des sciences, 1727, p. 9.
2. André-Thomas: Le réflexe pilomoteur, Paris, Masson & Cie, 1921.
3. André-Thomas: Presse méd. **32**:321 (April) 1924.

hand became warm again more speedily than the right. The reactions on exposing the hands to hot and cold air are also mentioned. Other decisive signs following changes in the sympathetic system exclusively are those noted in cases observed by Eppinger.[4] He examined five persons who had presented a unilateral Horner's syndrome for many years, in an attempt to learn whether the derangement thus indicated in the cervical chain of the sympathetic was not really more widespread, without giving prominent symptoms of such general involvement. Polyuria, which appeared on the normal side after a catheter had remained in the ureter for some time, was absent from the side on which the Horner's syndrome occurred; Eppinger concluded from this observation that the lesion in his cases involved much more of the sympathetic system than merely its cervical segment. In two other patients who had suffered cervical sympathetic lesions through injury to the neck this renal change was not demonstrable.

The chief complaints of the patient whose case we are reporting were pain in the right side of the chest and excessive sweating over the right side of the face, neck and chest and of the whole upper right extremity. A diagnosis of actinomycosis involving the right posterior wall of the chest close to the spine and probably the right lung was made by operation and by study of the excised tissue, in which the ray fungi were found. The roentgen ray disclosed an osteomyelitis of the seventh rib near its articulation with the spine. There was definite evidence of a change, probably irritative, in the sympathetic nerves or ganglia from the first to the twelfth thoracic, inclusive. The midline and the line of the right twelfth rib formed sharp boundaries to the area of altered sympathetic nerve responses. At the same time, no sign or symptom of sensory or motor change in the chest could be elicited, so that we felt justified in concluding that the effects were due entirely to alterations in the function of the sympathetic system. The only other suggestions of any neurologic change were a left hemiatrophy of the tongue, which, on protrusion, deviated somewhat to the left, and a slight diminution in the left pharyngeal reflex.

REPORT OF CASE

History.—S. I., a Russian iron worker, aged 43, entered Mount Sinai Hospital, Dec. 26, 1922, in the service of Dr. E. Libman, complaining of pain in the right side of the chest, with a slight cough and fever of one week's duration and one slight hemoptysis.

Examination revealed a well nourished man, acutely ill, with labored respiration, cyanosis and a hacking cough. He had slight exophthalmos, and the tongue was protruded to the left. There were signs of consolidation of the middle and lower lobes of the right lung. A blood count showed: white blood cells, 30,000, and polymorphonuclear cells, 88 per cent. The blood pressure was 120 systolic and 80 diastolic. The temperature varied, rising as high as 104 F., but was

4. Eppinger: Berl. klin. Wchnschr. **58**:1349, 1921.

usually from 101 to 102 F. Roentgen-ray examination revealed infiltration at the root of the right lung and osteomyelitis of the right seventh rib near its vertebral articulation, destructive, but no visible regenerative changes. The patient improved and was discharged on Jan. 23, 1923.

The man returned, Oct. 13, 1923, complaining of more severe pain in the right side of the chest for six weeks. He also had noted sweating of the right side of the head, neck and chest and of the whole right upper extremity. He now had: a slight, tender swelling in the right scapular region, dulness and diminished breath sounds over the upper part of the right side of the chest, sweating over the area described, left hemiatrophy and left deviation of the tongue, slight diminution in the left pharyngeal reflex and slight exophthalmos. Roentgen-ray examination showed an infiltration of the lower part of the right upper lobe and a more extensive lesion of the seventh rib in the area already described. It was during this interval that examinations of the sympathetic nerves were made.

The patient gradually improved, and went home on Dec. 5, 1923. He was readmitted to the hospital twelve days later with severe recurrence of the recent symptoms. The swelling in the right scapular region was opened on Dec. 18, 1923, by Dr. Neuhof in the service of Dr. Elsberg, and was found to be an actinomycotic abscess. The ray fungi were found in smears and sections. The patient progressed fairly well, and was discharged on Jan. 15, 1924. He was readmitted on Feb. 9, 1924, having lost appetite and weight; the only definite change was distinct clubbing of his fingers. He lost ground steadily, and died on Feb. 25, 1924.

EXPERIMENTAL OBSERVATIONS

Hyperhidrosis.—The right side of the face and neck, the front side and back of the chest down to the twelfth rib and the entire right upper extremity were covered with sweat most of the time, while the rest of the body remained dry. At intervals, when even the involved area was dry, the localized hyperhidrosis could be elicited by a subcutaneous injection of 1/6 grain (0.01 Gm.) of pilocarpine.

Goose-Flesh.—Goose-flesh could be produced on the right arm and on the right side of the chest by stroking either the spine or the right or left side of the back with ice. Under these circumstances, goose-flesh sometimes appeared subsequently—perceptibly later—on the left side.

Pilo-Erection.—Erection of the hairs on the right side of the chest, but not of the left, and on the right arm could also be brought about by stroking the spine or the right or left side of the back with ice.

Nipple Erection.—The right nipple frequently became erect spontaneously, while the left remained inert. Several forms of stimulation, such as light touch, exposure of the unclothed back to cool air or the touch of a piece of ice to any part of the spine would produce erection of the right nipple, but did not have a noticeable effect on the left nipple. Erection of the right nipple was usually accompanied by the appearance of goose-flesh on the right breast in a ring around the nipple.

Dermographia.—Drawing a pin across the chest with pressure sufficient to elicit slight pain produced a much more extensive reaction on the right side than on the left; the appearances on the two sides were sharply demarcated from one another at the midline. The red line appeared much sooner, spread to a far greater distance, and remained many minutes longer on the right side than on the left; a white line always preceded the red on both sides.

Ocular Changes.—At first, no differences could be detected between the eyes, which were slightly, though equally, exophthalmic. As weeks passed, the right

eye became slightly more protuberant and the right pupil slightly larger. The ocular and sweating changes were the only ones observed in the face.

Thermal and Vasomotor Changes.—Actual thermometric measurements were not made, the changes being so gross as to be easily perceptible to the touch. Usually the right hand and arm were cooler to the touch than the left in a room in which the temperature remained at about 68 F.

(*a*) The hands were immersed in water at 119 F., for three minutes.

Immediately on withdrawal from the water, the hands were equally warm. Observations made during ten minutes showed that the right upper arm became cold within a few minutes, and the cold area slowly extended, creeping down the arm, until it finally reached and involved the whole hand. Within a few minutes, the left hand, especially the fingers, became cold; they gradually grew warm again, the left finger tips being the last parts to reach the preexperimental status. The hand became a little pinker during the minutes following the immersion. No special change occurred in the arm.

End-Result: Both limbs were in the condition existing prior to the immersion, the left arm and hand being warm and dry and the right, cool and moist. The finger tips of both hands were the last parts to acquire the final temperature. About five minutes after the immersion, the right hand assumed a livid and mottled appearance, which persisted for some time.

(*b*) The hands were immersed in ice water for fifteen seconds.

Immediately on withdrawal from the water, the hands were equally cold; the right arm also became cold, and broke into a profuse sweat.

Observations were made for ten minutes. The right arm remained unchanged. The hand promptly became very warm and mottled (white spots on a reddish-purple background) and then remained unchanged for some time. The left arm slowly became warmer; the warmth crept down, gradually involving the hand. The fingertips were the last portion of either hand to become warm.

One hour after the immersion, the hands had returned to their usual state, in which the right was cooler and paler than the left. Definite differences between the sides of the chest were not made out.

Blood Pressure.—Essential differences were not detected between the blood pressures in the two arms.

Reaction to Epinephrine.—Definite differences were not discovered in the reactions of the two sides.

Growth of Hair and Nails.—The chest was shaved, and was observed until the hair had become plentiful again. No difference in the rates of growth or the quality of the hair or nails could be made out between the right and left sides. The rates of growth were tested by following the progress of scratches made on all the nails equidistant from their bases.

Electrical Reactions.—The reaction to faradic stimulation of the right and left pectoralis major, triceps and biceps humoris muscles and of the ulnar nerves did not present any differences. Galvanic stimulation of the ulnar nerves elicited the same responses on both sides.

COMMENT

In the case of André-Thomas the signs were, apparently, those of paralysis, while in our case they seem to have been irritative. In the two cases, the pilomotor and perspiratory observations were, as would be expected, opposite to each other. It remains to be explained, how-

ever, why certain vasomotor and thermal phenomena were identical in the two instances. It is true that in André-Thomas' patient the involved hand was usually warmer than the other, while in ours, it was cooler. However, the reactions to cold water and to stroking the front of the chest were, apparently, identical in the two. Studies on the reactions to hot water are not mentioned in this particular case of André-Thomas.

The patient died fourteen months after the onset of the symptoms. Observations on the status of the sympathetic nerves could not be continued beyond the first half of the illness. Unfortunately, permission for an autopsy could not be obtained, so that the ganglia were not examined histologically.

SUMMARY

1. A case of actinomycosis of the right lung and right posterior chest wall is described, in which disturbance of function of the thoracic sympathetic chain occurred; they were probably irritative. The area in which sympathetic changes were manifested included the right side of the face and neck, the entire upper right extremity and the right side of the chest down to the twelfth rib. The midline and the line of the twelfth rib formed sharp boundaries.

2. The sympathetic changes were indicated by localized hyperhidrosis, appearance of goose-flesh, pilo-erection and unilateral nipple erection, an exaggerated response to the drawing of a pin across the right side of the front of the chest, a lowering of the temperature, with pallor of the right hand as compared with the left, and bizarre responses of the upper right extremity to extensive changes in temperature. In a general way, the reactions of the right arm and hand were the opposite of those of the left.

3. No differences between the right and the left upper extremities were observed in blood pressure, growth or condition of the hair or nails, reactivity of muscles or nerves to electrical stimulation, nor in their reactions to epinephrine.

News and Comment

NINTH INTERNATIONAL CONGRESS OF PSYCHOLOGY

The Ninth International Congress of Psychology will be held at Yale University in New Haven, Conn., probably in August or September, 1929. The president of the congress is J. McKeen Cattell of New York.

This is the first meeting of the congress in America. The last meeting was held in Gröningen, in 1926. It is expected that the congress in the United States will be truly international in character.

ASSOCIATION FOR RESEARCH IN NERVOUS AND MENTAL DISEASE

The subjects for research which have been decided on and their dates are as follows:

1928. "The Vegetative System." Walter Timme, Chairman of Program Committee.

1929. "The Convulsive State." Stanley Cobb, Chairman of Program Committee. Also "Further Studies in Schizophrenia." George H. Kirby, Chairman.

1930. "Manic Depressive Psychosis." William A. White, Washington, D. C., Chairman of Program Committee.

THE AMERICAN NEUROLOGICAL ASSOCIATION

The Fifty-Fourth Annual Meeting of the American Neurological Association will be held in Washington, D. C., on May 1, 2 and 3, 1928.

POSTGRADUATE COURSE IN NEUROLOGY AND PSYCHIATRY AT VIENNA, SUMMER OF 1928

A second intensive course under the guidance of Prof. Wagner von Jauregg and Professor Marburg, and under the auspices of the American Medical Association of Vienna, will be given between June 1 and July 31.

Abstracts from Current Literature

GENERAL MEDICAL CONGRESS OF PSYCHOTHERAPY, BAD NAUHEIM, APRIL 27 TO 30, 1927. KANKELEIT, Arch. f. Psychiat. u. Nervenk. **81**:431 (Aug.) 1927.

This congress, at which 500 physicians representing the different branches of medicine (including those specializing in psychotherapy) were present, is a striking illustration of the interest in psychotherapy. The report consists of a series of abstracts of the papers read at the congress with some of the discussions that followed. They are divided under five headings:

1. *The Present Status of Psychoanalysis.*—This subject was opened by Schilder, a representative of the freudian school, who gave an outline of theories and policies. He adhered closely to the freudian conception even when it did not coincide with his own. He characterized psychoanalysis as a scientifically directed psychology which enables a grasp of psychic occurrences on a causal basis. Psychoanalysis concerned with those dynamic components of psychic life that can be scientifically appreciated even though life does not permit of an altogether scientific definition. The ego, super ego (ideal ego) and the id are considered as the main components of psychic life. The rhythmicity of instinctive life and the repetition—compulsion phenomenon—are stressed as fundamental. Schilder stated that psychoanalysis must adhere to the data observed and the theories advanced to interpret them. Attempts at fusion with other theories are unnecessary compromises that hinder progress in the search for scientific truth.

K. Goldstein discussed the relations between psychoanalysis and physiology. He used biologic analysis of changes observed in patients with organic lesions of the brain as the basis of an attempt to understand the phenomena that led to the establishment of psychoanalytic conceptions. This analysis has led him to take a critical attitude toward psychoanalysis. He stressed the point that function in health and disease should be considered on the basis of its relations to the whole individual and the situation in which he finds himself. The psychoanalytic school has taken isolated factors occurring in pathologic material and has utilized them in the construction of a theory underlying life in general. This theory not only is liable to lead one astray in the determination of the function of the human being in health, but tends to falsify understanding of the behavior of the whole individual even in disease.

Deutsch discussed the relation between psychoanalysis and internal medicine. Within recent years it has been realized that the development and function of the different organs are intimately related to instinctive life. As an organ develops, the part it plays in the instinctive life of the man as a whole serves to establish bonds between it and the sum total of his experiences. The symptomatology of disturbance in an organ is conditioned by these relations and can be fully understood only by a dynamic analysis of the instinctive life of the patient. Whether these relationships are manifest or hidden beneath the surface, the internist cannot afford to ignore them in evaluating the meaning of the symptoms. A knowledge of psychoanalytic principles and methods of approach will help the internist to discover such components and to adopt the proper attitude toward them even if the actual treatment may have to be left to those who have had a systematic training in psychotherapy.

The relation of individual psychology (Adler) to psychoanalysis was discussed by Kuemmel. He stated that the chief difference between the two theories lies in the fact that psychoanalysis is more scientifically directed. In line with other biologic sciences psychoanalysis seeks its object in a study of the libido, breaking the individual up into presupposed components. Individual psychology, as the name implies, is interested in the personality as

a whole, and looks for the cause of disease in the peculiar structure and relationships of the person in question. Individual psychology thus offers a more plastic and hopeful outlook and admits of a less fatalistic attitude.

In contradistinction to Kuemmel, Kogerer stated that more importance should be attached to consideration of the constitution of the individual. He regretted that as yet the constitutional type that predisposes to neurotic reaction has not been definitely outlined. The most important feature of such a constitution lies in a special oversensitiveness for disturbances in balance of the psyche, i. e., a pleasure-pain imbalance. He believes that in the normal person, a preponderance of pleasure over pain is responsible for a normal type of reaction. When this relation is changed neurotic reaction will result. This view would lead him to take exception to the freudian idea of a death instinct and of the repetition compulsion phenomenon in normal persons.

Mohr discussed the therapeutic determinants in psychoanalysis. The situation is complicated and cannot be schematically represented. The necessity of objective analysis of one's own personality, obedience to the analytic conditions, the acceptance of difficult situations, practice in free association, the positive influence of suggestion especially in the transference situations, the replacement of false guilt by a feeling of responsibility, and the replacement of narcissistic introversion by transference to the analyst, all play a part in the process. The discovery of dissociations makes for a desire for harmony. All these factors are present and the analyst can select and utilize those best suited to the individual case. In a similar vein Simmel discussed the various methods and their indications in psychoanalysis. He stressed the importance of the transference situation and its proper utilization. The analyst should take great care in the utilization of various factors at the proper time.

Hansen discussed some experiments undertaken for the elucidation of symptom evolution in the neuroses. It was possible to show that the suggestion of various types of food (carbohydrates, fats, proteins) under hypnosis influenced the quantity and quality of gastric and duodenal contents. He concluded that the neurotic symptom is of the nature of a conditioned reflex; an affect is conditioned to hinder or to stimulate a nonconditioned reflex (secretion).

Gerster presented an analysis of etchings in which psychoneurotic mechanisms appeared clearly. The creative ability of the artist served the purpose of free association in analysis and brought material up from an unconscious level.

2. *Psychotherapy and Therapeutic Pedagogy.*—Homburger discussed the attitude taken by the clinical neuropsychiatrist. He stated that in approaching the child one should not be guided by any preconceived theory. An analytic evaluation of the environment is important, but not more so than a similar appreciation of the child itself, that is, of its constitution. The psychoanalyst is hampered by his attitude to the neurotic adult when he approaches the child. Similarly the individual-psychologist (Adler) regards the child in the light of his preconceived philosophy of life. In both cases the constitutional factor is neglected, either methodologically or as a matter of principle. The child is to be considered as a world in itself in which education is indicated but in which one's philosophy of life must not be forced too far.

Representing the adlerian point of view, Weinmann finds the roots of asocial tendencies and difficulties in the upbringing of children, in the family milieu. The loss or inadequacy of either parent, quarrels between parents, overaffectionate or indifferent attitudes toward the child, and other such handicaps will make the child's adaptation to the home environment difficult, cause a twist in its life and will find expression in faulty adaptation in future life. In dealing with this difficulty it is advocated that one pay as much attention to the education of the environment as to that of the child.

In keeping with this idea, Allers stressed the adlerian concept of the environment as the most important factor in character formation. "There is

no born character although there may be a predisposition to certain developmental directions." This concept, he feels, renders the outlook of pedagogy and psychotherapy most hopeful in the early days of development.

Moos reported experiences with observation classes for psychopathic pupils in Zurich. In the special classes for "problem children" under the direction of teachers who were pedagogically and psychopathologically trained, both the personality and the environment of the problem child were analyzed. An attempt was made, on the one hand, to correct faults in the milieu, whereas, on the other, twists and handicaps in the children were either corrected or allowed for in a new adaptation. Some children, however, with more serious psychopathies were weeded out and placed in special homes or schools. The results so far have been good.

A similar hopeful outlook was reported by Seif who discussed the program and possibilities of the "education-advisory" clinics (Erziehungberatungsstellen). These clinics have been established by followers of Adler in different cities. Meetings are held under the guidance of individual-psychologists (mostly physicians) at which "problem children" are presented, their difficulties analyzed and the best management of the cases discussed by the physician or teachers and the parents.

Cimbal discussed a program for the organization of psychotherapeutic approaches of children in larger cities.

Puberty neuroses and psychopathies were discussed by Feuchtwanger. Many reactions which might be considered abnormal in an adult must be taken as part of the developmental process. These may, however, become pathologic if the youth does not grow out of them, or if they become exaggerated. These pathologic turns may be determined by some developmental conditions in puberty, or by dispositional factors carried over from childhood. In both cases an analytic approach will help in understanding the mechanisms and often lead to successful treatment. Such an approach will also correct the attitude of those concerned with the education of the child.

Simon stated that a combination of psychotherapy and education will be beneficial in the management of patients in the hospitals for mental diseases. An analytic appreciation of the prepsychotic personality with an understanding of the mechanisms of the psychoses will help in outlining the management of the case during the acute phase and will serve as a starting point for the re-education of the patient for return to society.

3. *The Clinical Aspects of Psychotherapy.*—Bunnemann brought out the value of psychotherapy in the treatment of skin diseases. It has been repeatedly shown that some lesions of the skin (urticaria, psoriasis, furunculosis, etc.) can be influenced by psychotherapeutic measures. The author also demonstrated that lesions successfully treated by suggestion under hypnosis can be made to reappear under hypnosis. He concluded that dysesthetic experiences and sexual conflicts, may be expressed in terms of lesions of the skin. These lesions can, in turn, be influenced by approaching the underlying mechanisms.

Schindler discussed the differential diagnosis, psychogenesis and psychotherapy of gastro-intestinal neuroses. One should not be satisfied with finding a psychogenic mechanism, but should first definitely exclude organic diseases. The different well known types (cardiospasm, proctostatic obstipation, cholangetic spasm, enteroptosis, psychogenic anorexia, diarrhea and other conditions) are discussed in terms of the mechanisms that bring them about, and forms of psychotherapy indicated. The methods applicable are the psychoanalytic, hypnotic, suggestive, and various others, but whatever method is used it should be reinforced by somatic treatment.

Durand Wever outlined the essential effects of suggestive therapy in cases of hyperemesis gravidarum.

The problem of bronchial asthma was discussed by Hansen. He finds two pathogenetic factors; an allergic diathesis, which he thinks is the exciting agent, and the degree of vegetative excitability of the organism. Whereas

little is known about the former, he considers that the latter depends greatly on psychic mechanisms and therefore presents the best point of approach. By psychotherapeutic measures he found it possible to raise the threshold against the allergy, thus helping the condition materially.

Lillienstein discussed the neurotic manifestations in the course of cardiac decompensations. He suggested the term cardiothymia for this type of reaction, which is conditioned by disturbances of the circulation in the cortex and brain stem. These disturbances can, however, be influenced by psychotherapeutic measures, thus avoiding a vicious circle in which neurotic manifestations aggravate the organic condition and vice versa.

The possible influences of psychic disturbances on the vascular system were discussed by E. Moos. Physiologically, fear and other emotions may influence the rate and pressure of the circulation. In nervous states continuous rises in blood pressure and rate can be induced. If allowed to continue for a long period, these rates may cause organic changes. Psychoanalytic treatment of the psychic disturbances will thus influence the organic condition.

Vauck presented the problem of the traumatic neuroses. These neuroses can be divided into those that accompany organic effects of trauma (and aggravate them) and those in which organic changes cannot be demonstrated. The latter may be precipitated by the trauma or may be caused by a flaring up of a previously existing condition. In all cases a thorough analysis, physical as well as psychic, must be undertaken before passing an opinion on diagnosis and compensation.

Hahn discussed the relation between neuroses and the endocrine chain. The results he has had with endocrine treatment of the neuroses led him to believe that psychic disturbances can be influenced by adjustments of endocrine glands.

4. *Reports of Commissions.*—Kronfeld reported on the activity of the commission for training in psychotherapy. Three subjects were discussed: (1) psychotherapeutic training of undergraduates; (2) postgraduate work in psychotherapy; (3) the training of specialists in psychotherapy. The conclusions reached were: 1. Special courses on the neuroses and their therapy should be instituted in the psychiatric clinics of the universities, special attention being given to psychoanalysis. 2 and 3. Postgraduate courses for the training of those who wish to specialize in psychotherapy should be available either at university clinics or at special institutes founded by adherents of recognized psychotherapeutic schools.

Friedlaender reported on the commission for the investigation of quack practitioners. Of all branches of medicine, physiotherapy and psychotherapy have suffered most from the invasions by such practitioners. The following plans are considered advisable in combatting this condition in psychotherapy: 1. Physicians who desire to practice psychotherapy must receive special training; 2. None but a physician should be admitted to the practice of psychotherapy.

Although the recommendations of the commissions were practically unanimously accepted, the discussion following the reports brought up the advisability of modifications. Many expressed themselves against considering psychotherapy a specialty in itself. The members felt that at the present stage all that could be done was to insist that study of psychotherapy was essential for the training of neuropsychiatrists.

5. *Further Contributions.*—Haeberlin discussed the value of religious experiences from a psychotherapeutic point of view. He pointed out that, parallel to the increasing tendency for specialization in medicine, an attempt to correlate medical methods with trends of more general interest has become noticeable. Examples of this are the cooperation of the physician with the teacher, and that between medicine and religion. One problem is whether religious experience can be utilized to influence pathologic conditions. The tendency for unity and harmony that characterizes religious experiences would be of great help in giving the patient a more hopeful outlook on life. Haeberlin urged the physician to make use of such experiences whenever possible.

Speer also advised more cooperation between the physician and the clergyman as, in many cases, such cooperation would result in closer approach to the mechanisms responsible for mental deviations.

Herzberg attempted to define the factors in the psychoanalytic situation that are responsible for its therapeutic effects. He stressed the point that bringing complexes into the patient's consciousness is not the only factor of therapeutic value. There is also the relation of the patient to the physician, the appreciation of the psychogenicity of the symptoms, the interest that the physician appears to take in the patient, the effect on feelings of guilt and inferiority, and others.

Schultz discussed the method devised by him some time ago which he calls "rationalized autosuggestive training." It consists in training the patient for introspection, something akin to "fakirism." The patient is trained to concentrate on introspection in relation with one organ, and then gradually to transfer this to the rest of the body — the voluntary musculature, the vascular system, etc. According to him this represents "a systematic physiopsychologic transformation of automatic functions into a rational appreciation." Autosuggestion plays a great part, but can be systematically controlled; the results obtained appear to be promising.

Hirschfeld spoke of a systematic milieu therapy. Analysis and treatment of the patient are not of value if the environment is not similarly analyzed and changed wherever changes are indicated and possible. The attempt to force the improved patient into his previous environment without its complete investigation may result in recurrence of the symptoms. In psychoanalytic procedures especially, the physician, who during the treatment represents an important part of the patient's environment, can help materially by gradual training of the patient.

Moerchen discussed the advisability of a more systematic approach to the concept of the neuroses from a practical point of view. He stressed the fact that some neurotic manifestations are as true of the normal state as of what is called a neurosis, and even of organic disease. He urged a clearer definition of the limits of disease in these concepts.

Lenzberg criticized current dream theories. From the individual-psychology point of view, the dream is a product of a more primitive form of thinking. The psychoanalytic concept that sees in the peculiar forms of the dream the activity of a censor and symbolic transformation is not justified.

Friedlander analyzed the Coué movement. This movement, given a scientific background by Baudoin, is still persistent among lay persons and is taken seriously even by some physicians. Critical analysis shows that the points brought up by Coué that cure is obtained by repressing the disease process into the unconscious; that when the will and imagination come into conflict the former succumbs to the latter are untenable. The methods used, especially that of mass treatment, are essentially unscientific.

The present status of hypnotism was discussed by Levy-Suhl. The newer psychotherapeutic methods have changed the attitude toward hypnotherapy, but it appears to have its place; recently, even the psychoanalytic school (Schilder) is beginning to employ it. Hypnotism is not used in the same sense as before, as a sympatomatic treatment, but for a better approach in analysis. The author agrees with the psychoanalytic interpretation of the hypnotic situation as a form of regression, but objects to the idea that the relation between the patient and hypnotiser is as closely akin to the sexual as the psychoanalytic school claims.

Staudacher suggested new methods in hypnotic treatment. With a knowledge of the patient's personality one could undertake a series of suggestive treatments under hypnosis with training in autosuggestion outside the hypnotic sessions.

In spite of the apparent dissimilarity in the theories and methods advanced by different psychotherapeutic schools, the fundamental issues were brought to

clear demonstration in the papers presented and in the ensuing discussions. This congress, like the first one, has shown conclusively that psychotherapy is gradually developing into a practical method of approach that will find its indication and applicability not only in the specialized field of neuropsychiatry, but also in the field of medicine in general.

MALAMUD, Foxborough, Mass.

NORMAL AND PATHOLOGIC SLEEP. LHERMITTE and TOURNAY, Rev. neurol. **1**:751, 1927.

Tournay gives a description of the physiologic condition of the body during sleep. He describes the diminished tonus of the muscles and the exceptions to this in the case of the hands, the ocular musculature, masticators and the sphincters. The contraction of the pupils, with upward and outward deviation, becomes more marked with the depth of the sleep, the tendon reflexes are diminished, and in very deep sleep the Babinski sign may become positive. Sensibility is reduced as a whole, the hearing being the last affected, and the transmission of nervous impulses seems to be slower. Inspiration becomes longer and deeper, expiration shorter, and the type of breathing is essentially thoracic, the relaxation of the diaphragm being associated with upward displacement. Occasionally, Cheyne-Stokes respiration is observed; the diminution in the tone of the palate may give rise to snoring. Pulmonary ventilation is reduced. The pulse is slowed by prolongation of the diastolic phase. The systole is slower and less pronounced and the blood pressure is probably lowered, particularly in the brain. Dilatation of the peripheral vessels is sometimes pronounced, probably due to relaxation of tonus. The secretions sometimes appear increased, but have not been measured. Under normal conditions the urine is reduced and the density increased. The temperature falls toward morning. Metabolism is lowered. The characteristic features of sleep, however, are easily altered and waking may occur suddenly, the condition contrasting with coma and narcosis.

The acts of going to sleep and awakening are treated with particular emphasis on the hypnagogic visions which apparently can be aroused by stimuli coming through various channels other than the visual. The same may be true of dreams that are characterized by marked emotional tone. It seems as though, according to Bergson, during sleep the mind abandons its selective quality and ceases to adapt itself to external conditions.

Two different attitudes are taken in regard to sleep: One is that it is due to intoxication by accumulated fatigue products; the other, that, according to Claparède: "We do not sleep because we are intoxicated or exhausted but in order to avoid being so." A hypothetic hypnotoxin renders sleep more and more necessary, but even though the person may stay awake forty-eight hours or more, from twelve to sixteen hours seems to be about all one can sleep at a stretch. This hypnotoxin if it is such, seems to provoke sleep not by intoxication, but by exciting the inhibitory reflex. The internal inhibition of conditioned reflexes and sleep, according to Pawlow, are one and the same process; and, when the cortex is removed, conditioned reflexes no longer occur, so that it is suggested that sleep is the throwing out of function of the cerebral cortex. On the other hand, decerebrate animals show periodic diurnal activity. Inhibition is a partial sleep, according to Pawlow, and it is restrained within narrow limits by the influence of various stimulations. On the other hand, sleep is inhibition spread over a wide area, the whole hemispheres, and even beyond that to the midbrain.

In considering pathologic sleep, Lhermitte devotes most attention to the narcoleptic syndrome, a symptom common to the most varied pathologic states, which has as its foundation an imperious irresistible need for sleep to which the subject succumbs in spite of his wishes. A graphic presentation of the syndrome is given by the author. He points out, however, that few studies

have been carried out on the patient while sleeping, and that even the condition of the reflexes is unknown. Narcolepsy is frequently associated with cataplectic attacks, which consist in the loss of all postural tonus, and which come on in response to stimuli of various kinds, even from stimulation of the sympathetic nerve. The physiologic state during these attacks has never been examined, but consciousness is preserved. Occasionally these narcoleptic attacks are associated with hallucinations. The differential diagnosis between narcoleptic and epileptic attacks is usually not difficult, but the epileptic condition may present narcoleptic states. Before making a diagnosis of idiopathic narcolepsy, however, a large number of conditions must be excluded, and, even in these so-called idiopathic cases, various deviations from the normal in the endocrines and elsewhere may be found. Symptomatic narcolepsies are observed frequently in cases of cerebral tumor, independent of type or location, but the frequency of these attacks with tumors impinging on the third ventricle is impressive, so much so that the author states this fact should "stimulate us to seek in this region a center that possesses a preponderant influence upon the function of sleep." Narcolepsy as a complication of infectious diseases of the nervous system is also treated, syphilis and multiple sclerosis being especially noted. (It seems curious that narcolepsy following encephalitis is not mentioned.) Narcolepsy may follow traumatic lesions in which the skull is not fractured and in which evidence of injury to the brain does not persist. Narcolepsy may also accompany endocrine disorders, particularly hypophyseal, but it seems probable that this state occurs only when the region of the third ventricle is disturbed. Lhermitte, however, calls attention to the frequency with which narcolepsy occurs in obese persons and speaks of the analogy between adipose tissue and endocrine glands, referring to fat as the hibernating gland. Narcoplepsy as a manifestation of autointoxication is seen possibly in diabetes, but is easily differentiated from the condition occurring in other diseases. In hysteria sometimes there are paroxysmal attacks of hypersomnia, but, as a rule, the physiologic condition is far different and readily distinguishable. Tendency to continuous sleep is always symptomatic, and the easily reversible state between waking and sleeping is one of the diagnostic features, for a sleep that cannot be broken is not sleep but coma, and sleep that is interrupted but during which the patient is only partially conscious and slips back quickly to unconsciousness is more suggestive of stupor. Such tendencies to sleep are found in cases of tumor of the brain particularly those affecting the third ventricle, and in epidemic encephalitis, and may occasionally be found in syphilis and in simple arteriosclerosis.

A case of idiopathic narcolepsy has never been completely studied at autopsy, but cases of symptomatic narcolepsy with anatomic investigation are now fairly numerous. It is possible to localize the center responsible for this condition of narcoplepsy in the hypothalamus and the tegmentum of the mesencephalon close to the third ventricle and Sylvian aqueduct. Recent experiments by Demole have tended to show that normal sleep can be produced by the injection of minimal quantities of calcium chloride into the hypothalamic region between the optic chiasm and the infundibulum. The injection of 0.25 mg. of calcium chloride will produce sleep presenting all the characteristics of the normal and lasting from thirty to forty minutes. By injecting potassium chloride in the same doses and in the same location, reverse results are obtained. It has been shown that the only marked change in the blood during sleep is the reduction of calcium and potassium. It was, therefore, suggested that these elements acting on the hypothalamic region determine this state of more or less complete generalized inhibition of the brain.

In the discussion Piéron said that during sleep the electric resistance of the skin is increased, reaching its maximum shortly before waking and falling at that moment. In the cerebrospinal fluid of an animal prevented from sleeping there is a substance which, on injection into the fourth ventricle of a normal animal, brings about the same imperious need of sleep as in the donor. This

hypnotoxin is precipitated by alcohol, is soluble in water, does not dialyze, and is destroyed by heat and oxidation. Sleep seems to be an inhibitory defense of reaction against this intoxication. Possibly in some cases there is a disorder of metabolism which causes the formation of this toxin more rapidly than is normal.

Babonneix and Widiez reported a case of glioma of the corpora quadrigemina, with somnolence as the principal characteristic.

Henry Meige, in discussing sleep in art, showed several photographs of paintings and sculptures, and pointed out certain features that did not agree with scientific observations.

Claparède believed that there is an instinct of sleep revealing itself in the character of anticipation which is common to instinctive acts. Just as the swallow migrates before it is frozen, and the bird makes its nest before laying, so sleep strikes the patient with inertia before he comes to the stage of exhaustion.

Von Economo said that cerebral sleep seems to differ from corporeal sleep. It is characterized by a partial block of centripetal and centrifugal stimuli and by reversibility. The center controlling cerebral sleep seems to lie in the hypothalamus, close to the basal ganglia, and it seems to act especially on the cerebral cortex by some process of inhibition. Various experiments have been performed to localize this center more exactly; Demole found it close to the mammillary bodies; Mehes found it in the sylvian gray matter, infundibulum, and walls of the third ventricle; whereas Spiegel and Inaba produced sleep by destroying the lateral part of the thalamus. Sleep would seem, for the following reasons, to be controlled by two areas:

1. Decerebrate animals show spontaneously the same periodic swing from sleep to waking.

2. Certain hypnotics like bromides, alcohol and paraldehyde, which affect the normal, do not act on the decerebrate animal.

3. Chloral hydrate, phenobarbital and others act on decerebrate animals even more vigorously than on normal animals.

4. Such drugs as act on the inferior center act also on the temperature and on the vomiting center.

5. Scopolamine is ordinarily ineffective in the rabbit and cat, but dosages of 10 mg. produce profound sleep in decerebrate animals.

6. If magnesium sulphate is injected into a normal animal or into a decerebrate one, both animals go rapidly to sleep. If calcium chloride is then injected the sleep of the decerebrate animal becomes profound and all the reflexes disappear, whereas the normal animal wakes with a start.

One may conclude from this experiment that the forebrain and the brainstem react differently to certain chemical stimulants and depressants. Clinical medicine should learn to profit by these experiments in trying out various combinations of drugs that act on the cerebrum and on the mesencephalon.

Albert Salmon discussed sleep as a vegetative function in relationship with the endocrine and sympathetic systems.

Souques discussed the differential diagnosis between symptomatic and idiopathic narcolepsy, whereas Lhermitte and Rouques pointed out the relationship between narcolepsy and encephalitis.

V. Demole recounted his own experiments with the injection of minimal quantities of calcium chloride and of synthetic hypnotics into various parts of the brain. He believes the pharmacodynamic experiments reveal two anatomic components of the nervous system controlling the phenomena of sleep, a vegetative region lying close to the infundibulum, and a cortical component responding to psychic influences. Somnolence in tumor of the brain is probably due to direct or indirect mechanical pressure on the vegetative centers of the infundibulum controlling sleep. He also reported some cases of experimental catatonia in which the injection of small amounts of calcium

or potassium chloride into the thalamus from 7 to 10 mm. from the midline produced stupor, waxy flexibility and catatonic phenomena. "These facts, which speak in favor of the organic nature of catatonia, emphasize the puerility of the psychogenic explanations. The time is near when it will be possible to bring about at will experimental catatonia."

Jarkowski spoke of the influence of sleep on hypertonia and hyperkinesis, showing that usually these disorders yield during sleep. He also mentioned the recurrence of sleep on the injection of air into the cerebral ventricles.

Hesnard gave a psychiatric touch to the discussion.

Courbon, under the attractive title of "Night and Sleep in the Insane Asylum," discussed rhythms of sleep and came to the conclusion that among these patients sleep is short and light, with absence of motion and with the element of surprise at sudden awakening. Excited persons are pleased at this lack of sleep, the demented ones do not care, and the others are distressed. Other reactions toward sleep or the lack of it are discussed. Lindbergh was mentioned as an example of voluntary abstinence from sleep. A case of dissociated sleep was discussed by Rétif from observations of sleep on himself. Bourguignon reported the variations in the chronaxia in different functional states, both spontaneous and experimental, accompanied by organic lesions. In cases of simple schizophrenia modification in the chronaxia is not noted. Where cyanosis and goose flesh are present, the contraction slows down and the chronaxia increases to ten or fifteen times the normal value.

FREEMAN, Washington, D. C.

THE SIGNIFICANCE OF OXIDIZING AND REDUCING TISSUE FERMENTS IN CEREBRAL LOCALIZATION. MAX BIELSCHOWSKY and MAXIMILIAN ROSE, J. f. Psychol. u. Neurol. **33**:73, 1927.

The presence of oxydases in tissue elements not only furnishes good insight into the micromorphology of the living cell but is an indicator of certain metabolic processes within the cell body. Winkler was the first to demonstrate bluish granules in the protoplasm of lymphocytes after they had been stained with weak solutions of alpha-naphthol and dimethylparaphenylendiamin. This staining reaction, which is brought about by indophenyl blue synthesis, occurs only in cells which contain oxidizing ferments (oxydases). The application of these syntheses to microscopic examinations of fresh body tissues was further elaborated by W. H. Schultze, Gräff and von Gierke and Pighini, the last being the first to utilize the method in studying the central nervous system. Marinesco improved and perfected the technic so that he was enabled to study embryonic and pathologic tissues. He was able to show that, in abiotrophic processes in ganglion cells, the number of bluish granules found after staining the cells by this method paralleled the severity of the changes in the cells. His observations were especially interesting in cases of amaurotic idiocy; in this disease, the granules were found only in those parts of the cells that did not show pathologic storage of lipoids. Marinesco employed the method also in the study of processes of reaction in peripheral nerves. The results obtained by this method of staining furnished valuable confirmation of the results obtained by staining with silver.

Bielschowsky and Rose employed this method in efforts to solve some problems of localization in the cerebral cortex. They began with the idea that oxidation processes in the various layers of the cortex, as well as in its different areas, might show variations that could be utilized as an index of the activity of these areas. Marinesco had already shown that the various laminae in the motor area showed different oxydase pictures; the first layer was poorly stained, whereas the deeper layers appeared strikingly darker; in the fifth layer, blue granules were seen only in the portions of the cell bodies that were free from pigment; there was an especially rich deposit of blue pigment in the dendrons and pericellular axon textures in the second and

third layers. These observations were practically confirmed by Bielschowsky and Rose in their examination of the brains of five dogs and one monkey. Marinesco thought that the neuroglial cells contain oxydase only during embryonic life and only as long as histologic differentiation of neighboring nerve fibers was necessary; they disappear soon after this period. This observer never found blue granules in healthy brains; this naturally raised the question as to how these cells carry on their respiratory function. He advanced the hypothesis that this function was carried on by the peroxydases and iron ions—two elements which had to be taken into consideration in the respiration of nuclei of the cells that were free from oxydase. The stained sections proved that the peculiar and striking appearance of the third layer was not due exclusively to the presence of nerve elements, but that the glial symplasma of the adjacent gray substance had something to do with the nutrition of the nerve elements. The great vulnerability and the almost total disappearance of this layer is so-called cerebral hemiatrophy lends great support to this theory; the fact that the oxydase content of this layer is so strikingly increased is also suggestive of a specially increased need of oxygen by its nerve elements. The relatively poor oxydase content of the deeper layers of the cortical white matter is in harmony with the anatomic pathologic fact that these layers are more resistant to many of the circulatory disturbances. Almost identical conditions are encountered in the cerebellum; the molecular layer takes the stain unusually well, the granular layer less well and the layer of Purkinje cells assumes an intensity between these two.

Bielschowsky and Rose think that one fact is definitely established, namely, that the intensity of the oxidation process varies in the different layers of the cerebral cortex. They then undertook to determine whether there were differences in the oxydase content of neighboring cortical areas, and used Ammon's formation for this study. Rose had already shown how differentiation of the cortex of this structure occurs as one ascends the mammalian scale. Topographic conditions in the cortex of this structure are obvious; the cortex can actually be seen to consist of two layers. In the dog, Rose was able to distinguish five separate areas in the formatio ammonis; in man, the architectonic structure was practically the same. In addition to the fascia dentata (which consists of small granular elements) and subiculum, there exist five subareas which Rose designates h-1, h-2, h-3, h-4 and h-5. Area h-1, immediately adjacent to the subiculum, is recognized in Nissl preparations by its relatively wide area and the fact that it consists almost exclusively of medium sized pyramidal cells which become denser and denser as the zonal layer is approached. Area h-2 is characterized by the great affinity of its closely packed pyramidal cells for the basic aniline dyes; in silver preparations these cells are striking because of their long and dichotomous dendrons. Area h-3 is wider; its cells are smaller and more loosely packed together than the cells in h-2. Still looser and more irregularly arranged are the cells in h-4. Area h-5 is made up entirely of widely scattered cells within the hilum of the fascia dentata.

The indophenol-blue reaction gave the following results: Areas h-3 to h-5 appear different from areas h-2 and h-1; the latter take the stain much better than the former. The fascia dentata is usually well stained; its cells and their prolongations are filled with unusually large blue granules. Under higher magnification, it was evident that although h-1 and h-2 appeared about equally well stained, the deposition of blue granules in h-2 was limited exclusively to the ganglion cell bodies and their prolongations; in h-1 the intracellular gray substance participated strongly in the reaction. It was also evident that the symplasma constituting the glial ground substance in h-1 is, in contrast to the adjacent areas, much better developed; it is on account of this that the ganglion cell bodies and their prolongations in h-1 also appear less distinct.

These observations show a definite parallelism to the usual anatomic pathologic conditions found in this area. In general, h-1, which corresponds to the so-called Sommer sector, is a highly vulnerable cortical area, especially in genuine epilepsy in which the light color of its cell content and the sclerosing

"fuzziness" of the entire area makes it appear unusually pale. According to Bielschowsky and Rose, these observations in association with the fact that in this area the intracellular gray substance is relatively richer in oxydase than in the adjacent areas, could be utilized as an index of higher cortical differentiation. Similar manifestations in the third layer of the cortex would seem to confirm this hypothesis. Rose reached the same conclusions from phylogenetic studies. He found in the mammalian series that it was in h-1 that there is a tendency to a high degree of development which reaches its highest stage in man. The micromorphologic picture of fixed specimens is therefore in harmony with the results of the oxydase reaction. It would seem that in the indophenol-blue reaction one may have a ready index of functional differentiation.

The authors also compared the results of the indophenol-blue reaction with those of vital methylene blue staining. In the latter, the staining of the ganglion cells and their prolongations is a reduction process which gives rise to pictures closely resembling those obtained by the Golgi and the Cox methods of staining. The dye is reduced in the cells to a leukobase which does not become oxidized again to methylene blue until the oxygen of the air exerts its influence post mortem. The leukobase reaction is due to reducing ferments which affect the cells and their prolongations. For this comparative study, the authors used the brains from a few rabbits. The brains showed the greatest number of stained cells in the deeper layers of the cortex (the fifth and sixth); this was in marked contrast to the third layer, which showed most intense staining with indophenol blue. From this the authors conclude that the vegetative functions of the cells seem to be controlled more by oxidizing, on the one hand, and by reducing ferments on the other. In addition to this, the brains from the rabbit showed, with vital methylene blue dye, an especially intense staining of Brodmann's areas 4 and 6—the very areas which, in this animal, contain the corticomotor regions. The third layer also showed a considerable number of stained cells; this may have been due to the fact that many of the animals thus injected perished from convulsions, and it is possible that the intense degree of staining is an expression of an increased antemortem function of this layer of the cortex. The investigations on this phase of the problem, however, have not been concluded and will be the subject of a future communication.

KESCHNER, New York.

DISCUSSION ON LAY PSYCHOANALYSIS, Internat J. Psychoanalysis **8**:2 (April) 1927.

These contributions may be considered in their national groupings. Ernest Jones, Rickman and Edward Glover are the British contributors. Although differing considerably on many details, they are of the same opinion as to general principles. Jones' brilliant and thoughtful paper asserts that psychoanalysts have the choice whether they wish their science to exist under the aegis of medicine or to be in the hands of laymen. He stresses the real bonds existing between medicine and psychoanalysis, expressing a fear that a decision that medical training is "irrelevant" for the practice of psychoanalysis would end by making it so, and that psychoanalysis as a technic would then bear the same relation to the body of medicine as do pharmacy and massage. Jones believes that, occasionally, a lay analyst is as good a practitioner as the medical analyst, and therefore thinks a place should be found for him; however, in his work the lay analyst should never be independent of the physician. Jones finds that few laymen continue to work under medical supervision, and is therefore of the opinion that all who wish to become analysts should be urged to obtain medical qualifications. Realizing, however, that this will not be expedient in all cases, he believes that a strict selection should be made by those in authority, in respect to personality, character and previous scientific training. Rickman, while tacitly assuming that psychoanalysis is a profession distinct from medicine, emphasizes that "the candidate must have taken a definite step in the direction of scientific method before he can be admitted to the ranks

of professional analysis." Diagnosis must be left to the medically qualified, but authority denied the physician to prescribe the minutiae of treatment. Glover decides that, although the layman has a place in applied psychoanalysis today, when a modified medicopsychoanalytic course is feasible in the future, medical qualification should be exacted of those desiring to do therapeutic analyses.

The papers of the American group, consisting of Oberndorf, Brill, and Jelliffe, as well as the resolutions on the subject by the New York Psychoanalytic Society, present a united front in opposition to the admission of the layman into the therapeutic field. Oberndorf's paper is the most extended and the most comprehensive, and an abstract of it may be said to represent fairly the American point of view. At the outset he attacks the validity of the position taken by Freud that psychoanalysis is a science complete in itself and that the trained lay analyst is no layman in analysis. Such attitudes in this country, when applied for example to osteopathy, have served "as an entering wedge for the unskilled and inefficient to extend their activity into fields where they are unqualified and harmful." Agreeing that the physician without special training cannot do psychoanalysis properly, he feels just as strongly that the nonmedical analyst is disqualified from treating the neuroses. Medical training enables the analyst to diagnose more correctly, to interpret ailments occurring during analysis more accurately, as well as to make the important differential diagnosis between psychosis and neurosis. Besides all this, psychoanalysis is peculiarly adapted to quacks, since a critical third party cannot be present, and since physical interference does not take place which might result in demonstrable injury and on which suits for damages could be based. The public must be protected from such possibilities. Jelliffe's paper adds the interesting point that, having experimented for fifteen years with delegating patients to lay assistants, he has come to the conclusion that the technic should be left in the hands of the analytically trained physician.

There are seven German contributors. All are more receptive to the general notion of allowing laymen to do therapeutic work than are the Americans, and rather more so than the British. The group that seems definitely to favor lay analysis includes the important figures of Sachs and Alexander. Alexander, who may be made the spokesman of this group, opens with a belligerent accusation that medical analysts overemphasize their medical status because they are overcompensating for the stinging contempt of the medical profession toward psychoanalysis. He follows this attack with the remark that physicians are incapable of giving treatment for mental ailments, and points to the fact of lay analysis in proof of this assertion. Believing that the lay analyst and the nonanalytical physician are alike "transitory phenomena of our age," the result of the onesidedness of medicine of our day, he looks forward to a time when "the science of the personality and the knowledge of the body will stand side by side as two parts of the whole, equal in value and complementary to one another." In the present nonmillenial age, however, "psychoanalysis needs medicine less than medicine needs psychoanalysis." Muller-Braunschweig, with much the same point of view, comes to the conclusion that all the analytic therapist requires is his one sided psychoanalytic training, while the analytic scientist or researcher requires a far broader one, including medicine. Sachs argues that if he is entitled to his place in the Berlin Lehrinstitut, where he gives didactic analyses, he, being a layman, also has a right to do therapeutic analyses, since he sees no essential difference between them. Benedek believes it would be fatal to the science of psychoanalysis to lose its lay workers and depend wholly on medical analysts. Her dictum is that in the countries that permit it, lay analysts will flourish in any case; in those countries where there are laws against it, the International Psychoanalytical Association should strive for legal recognition.

Differing from these contributors, Simmel and Horney express views favoring a medical training for psychoanalytic therapists. Simmel, in an extensive paper, enumerates the many reasons favoring such a training. He mentions

the "continuous reciprocal effect" of psyche and soma, and stresses the importance of knowing the soma. Furthermore, with regard to the handling of intercurrent ailments, a consultation with another physician "should not take place because of any incompetence on the part of a lay analyst, but because of a voluntarily expressed recommendation on the part of a medical analyst." He concludes that in carrying out analytic treatment, medical qualifications "are not matters of indifference" to the practitioner, and that "the possibilities afforded by a knowledge of medicine enable him, both before and during the analysis, to meet, with a full sense of his own personal responsibility, the demands made by so many-sided a problem as disease."

The group in Vienna, the cradle of psychoanalysis, under the influence of Freud, who so strongly endorses lay analysis, offers nine contributions. Of these, four, those of Reik, Nunberg, Wälder and Jokl, definitely favor lay analysis. Reik, a doctor of philosophy, with some show of finality places psychoanalysis as a branch of psychology rather than of medicine, and regards therapy as merely one application of it. Hence the term "layman" applies in psychoanalysis to the neurologists, psychiatrists and academic psychologists. Further, the forerunners of scientific psychoanalysis are not to be found in the chairs of the learned faculties of colleges, but in the ranks of the philosophers, writers and clergymen. Nunberg and Jokl, both physicians, offer arguments similar to those of Alexander. Wälder frankly states that he has a prejudice in favor of lay analysis, which he places to the credit of his liberalism, and writes the following remarkable sentence: "It is certainly not honorable to drag in the interests of third parties; the community does not protect its members from the manifold hygienic, material, social, and mental dangers of life, and it is not comprehensible why it should take up the task of protecting them from the possibility of even real quackery."

Three of the Vienna group, Sadger, Hitschmann, and Schilder exclude the layman — rather categorically — from the treatment of the neurotic adult. Sadger leaves an opening for the lay analyst in the treatment and education of children and adolescents, and feels that the lay analysts have, particularly the female ones, advantages over the physician in treating such persons.

The Dutch group, represented by the contribution of van Ophuijsen, believe that the practice of psychoanalysis should not be allowed to persons without medical training, and that the patient's interests are inadequately safeguarded by the supervision of a medical man.

The Hungarians are represented by a contribution of Roheim, an anthropologist, who expresses the belief that the broader studies requisite for analytic training will be best available "if we do not cut the threads which connect us with the various nonmedical branches of science." The Hungarian Psychoanalytic Society regards the whole question as already settled, since Freud favors lay analysis, and since in Hungary lay analysis has never resulted in injury to any patient. Accusing the unanalyzed medical analysts of bringing the matter to an issue because they feel the necessity of economic competition with qualified lay analysts, the members demand legal and other support for lay analysts by the International Psychoanalytical Association, whenever they come in conflict with the law.

SILVERBERG, New York.

A PHYSIOLOGIC CONCEPTION OF HYSTERIA. L. BLUMENAU, J. f. Psychol. u Neurol. **34**:243, 1927.

The present conception of hysteria is that of a psychoneurosis in which the somatic symptoms are to be interpreted psychologically and not physiologically. Blumenau asks: "How can one explain the conversion of the psychic component into a somatic one?" "How can one explain a hysterical paralysis following fright?" Paralysis—an objective somatic phenomenon—and fright—a subjective experience, a state of consciousness—cannot be separated from each other; some transitional process that connects the paralysis and the fright must

occur. Pawlow was the first to demonstrate dissociation which after all is the basis of hysteria in the experimental animal, as manifested by loss of previously formed conditioned reflexes—by "dissolution" of temporary cortical associations. This cortical process is designated by Pawlow "internal inhibition" in contrast to "external inhibition," a phenomenon common to the entire nervous system and occurring in one center during stimulation of another. The precise nature of this inhibitory process is unknown, although, thanks to the researches of Pawlow and his pupils, many of the characteristics of this phenomenon are well known. Internal inhibition sets in much sooner than exhaustion, so that it would seem to act as a protective mechanism by preventing exhaustion of the cerebral cortex. A previously experienced intense stimulus is sufficient to set this mechanism into active operation. Under certain conditions a less intense stimulus may have an inhibitory effect; this is especially illustrated by the so-called "conditioned inhibitions." Pawlow showed experimentally also that inhibition "irradiates" and may extend to surrounding areas in the form of "induction." In this way certain parts of the cortex which have not as yet been "exhausted," and not even stimulated, may be inhibited by "irradiation."

From these facts it may be concluded that internal inhibition does not indicate a passive failure of exhaustion, but rather an active mobile process which acts like a stimulus, though in an opposite direction—it represents a sort of active dissolution of temporary cortical associations. Like a stimulus, a previously diffuse inhibition will also become concentrated in certain definite areas. As a matter of fact, even a normal brain may be affected by this form of inhibition, although irregularly and with an intensity varying from moment to moment; when this form of inhibition affects the entire cerebral cortex, it leads to the phenomenon of sleep. According to Pawlow, sleep and internal inhibition are identical processes.

Hysterical attacks may occur without loss of consciousness. Clouding of consciousness, however, is a characteristic feature of hysteria which resembles hypnosis and is therefore designated as a hypnoidal state. The hypnotic state itself has long been recognized as an artificially produced partial sleep in which the sensory centers may be wide awake (or partially so), while the higher associative mechanisms of the cortex (such as logical thinking) are more or less in abeyance. Even in the waking state hysterical persons also show manifestations which can best be explained on the theory that they are the results of a chronic partial inhibition of cortical functions. Hysterical amnesias, anesthesias, paralyses, mutism and similar symptoms represent a protracted concentration of the inhibitory process in individual cortical centers or mechanisms.

The crux of the entire question, however, is: What is inhibited in hysteria; is it proper to speak of inhibition of certain cortical centers in hysteria? The cerebral cortex contains clearly outlined sensory and motor centers; besides these, there exist less circumscribed areas for simple monosensory associations, such as the sensory, motor and graphic speech centers. Strictly speaking, localization does not exist for higher associative activity; there are no centers but merely associations of many neurons which are diffusely scattered over the entire cortex. Disturbance in this associative activity must be regarded as the cause of hysteria; symptom-complexes referable to inhibition of definite cortical centers cannot be demonstrated. Hysterical anesthesias and akinesias are due to a dissociation of association complexes which represent individual parts of the body or individual functions (such as speech and gait) as a unit. Although it is true that the akinesias and anesthesias correspond to definite parts of the body or to the functions of such parts, they are not due to a true loss of these functions because the loss is merely a psychologic manifestation of their dissolution. Motor and sensory aphasia due to lesions of the cortical centers are not symptoms of hysteria. Mutism is a manifestation of a general, higher level. That there is no disturbance of the function of the speech center in hysteria is evidenced by the fact that mute hysterical patients talk well during sleep or when in a state of clouded consciousness.

One is not dealing, therefore, with inhibition of cortical centers but with intercentral, intracortical inhibition—a dissolution of temporary associations. In intracortical inhibition, the function of the centers is not lost but is split off from the great association complexes which are the substratum of personality. One may assume that in every case of hysteria there occurs a direct primary intracortical irritation; any affective state—a depression, an emotional episode—may be the exciting cause of hysteria, and the point of the irritation must be in the cerebral cortex. Although the subcortical ganglia (thalamus and corpus striatum) may be the actual centers of psychic reflexes and of emotional expression, and although the same centers can also react autonomically to simple pain and hunger stimuli, as in the new-born, during emotional episodes—fright, grief, anger, doubt—the stimulus or irritation must originate in the cortex.

The cortical association complex which is primarily stimulated in such cases represents the irritative focus of the cortex; it must not be regarded as a limited focus but rather as an extensive network of contiguous cortical neurons. It is by induction (Pawlow) or energy absorption (Lipps) that such a focus is the starting point for an inhibitory process which affects the surrounding cortical mass. This explains the disturbances in the operation of logic and in consciousness during severe affects. Under normal conditions, this disturbance in equilibrium is quickly readjusted, first through the discharge of energy from the focus of irritation to the subcortical centers (psychoreflex abreaction), and later through irradiation of the stimulus from that focus toward the association tracts and through inhibition of the focus by other cortical neuron complexes (associative, psychic abreaction). In the hysterical person, on the other hand, owing to a conditional weakness of the associative mechanism (lack of psychic synthesis), this adjustment is incomplete, and the focus of irritation is not extinguished but keeps on smoldering, being lighted up from time to time by psychic irritative phenomena or convulsive attacks; the inhibition induced in the surrounding cortex does not disappear but becomes less diffuse and more concentrated in individual systems and gives rise to certain symptoms (such as amnesias, anesthesias and akinesias).

It is not always easy to explain why inhibition remains concentrated in one or the other association system. It may be said that: (1) Prolonged inhibition frequently affects those systems that have been strongly inhibited during the exciting affective experience. Thus, a momentary inability to run during fright may become fixed in the form of an abasia or even a paraplegia, an inability to cry out, as aphonia or mutism. In this category may also be included the anesthesias, the amnesias and the numerous cases of hysterical deafness following explosions. (2) Frequently, the functions inhibited are those that have been in action during the period of nervous shock; a psychic shock experienced while eating may be followed by chronic anorexia or obstinate vomiting. (3) Frequently, the functions inhibited will be those that have previously been impaired by disease or exhaustion. Here may be included the cases of psychic aphasia following a slight laryngitis and the numerous hysterical complications encountered as superadditions to organic disease. The frequent recurrence of symptoms in hysteria can thus be explained by changes in the resistance of the corresponding systems that have been below par. (4) Of special importance in hysteria is the individual structure of the temporary associations which directs the inhibitory process in various directions that cannot be readilly followed. In this group belong cases similar to the one reported by Breuer in which the patient developed a hydrophobia-like condition after seeing a dog drink water from a glass.

To summarize: Hysteria is a disturbance—predominatingly an inhibition, occasionally a dissolution—of temporary cortical associations; it is a type of conditioned neurosis. Congenital associations are not affected in hysteria; unconditioned reflexes, as a rule, are retained. Associations acquired by a patient in the course of individual life experiences do not, as a rule, fall apart; more often they are completely split off from the extensive cortical complex

(personality) in order to reestablish themselves just as completely. In hysteria there frequently occurs a narrowing of the personality; occasionally a division, but never a dissociation as in insanity.

KESCHNER, New York.

APHASIA SYSTEMS. S. E. HENSCHEN, Monatschr. f. Psychiat. u. Neurol. **65**:87 (June) 1927.

The author devotes ten pages to an interesting summary of the historical development of the study of aphasia, giving briefly the position occupied by each of the great early investigators, his contributions and his mistakes. He then gives a critical analysis of the recent work of Head, "Aphasia and Kindred Disorders of Speech." Head's work is an attempt to develop and expand the ideas of his teacher, Hughlings Jackson. The work has the inherent defect of being based purely on clinical investigations; and, in spite of the fact that the case studies are exceptionally well done, they lack a fundamental pathologic basis on which alone one is justified in building a theory of localization, or of judging its value.

Head divides the aphasias into four groups; verbal, syntactic, nominal and semantic. The first group, verbal aphasia, obviously corresponds to Broca's aphasia. In four cases of this group, the lesion is clearly in F^3, and these four present an unusually pure clinical picture of Broca's aphasia. In spite of Head, they prove that there is an exact and constant localization of the Broca type. In the other clinical cases of this "Verbal" group, the symptoms are the same. As they are chiefly cases of vascular disease, they are useless for any accurate localization of the lesion; nevertheless they show, in spite of Head's denial, that there is a clinically isolated Broca's aphasia (with agraphia).

Of syntactic aphasia Head says, "An easy form to distinguish, because the patient tends to talk jargon—the rhythm is defective—and there is want of grammatical coherence." There were three patients in this group; all showed jargon speech. Word deafness was fairly marked in one, and was very slight in the other two. Head's position that there is no localization for jargon aphasia is untenable. These cases correspond to the temporal aphasia of the localizationists. There are many similar cases in the literature, where, in spite of a lesion in the medulla of the first temporal convolution, no word deafness is found. It is to this group that Head's cases belong. They are not cases of pure temporal aphasia. Two were complicated by apraxia, certainly as a result of injury to the second parietal convolution. One was complicated by mild word blindness and agraphia due to a more extended lesion. But in the absence of pathologic examinations, the course and effect of the bullet cannot be exactly determined.

Three cases of nominal aphasia are reported. They are characterized by inability to find names for objects, by word blindness and by agraphia. One case, a vascular lesion, is not of value for localization; in the other two the lesion involved the angular gyrus. In one of them the parieto-occipital zone was also affected. These are cases of typical angular gyrus syndrome—amnestic aphasia, word blindness and agraphia. The associated disturbance of form sense is readily explained by involvement of the occipital lobe. Discussing angular gyrus lesions, Henschen points out that in the triad of symptoms, word blindness and agraphia are the important ones; amnestic aphasia is much less so. Amnestic aphasia has in itself no localizing value, as it may occur as a part of motor aphasia, as a part of a temporal lobe aphasia, and, as Pitres showed, even as a result of left parietal lobe lesions. In other words, amnestic aphasia occurs in all types and localizations of aphasia; it is not a special or isolated form of speech disturbance.

Eight cases are described under the heading of semantic aphasia. They are not cases of aphasia. There is neither motor aphasia (aphemia or

agraphia) nor sensory aphasia (word deafness or word blindness). The patients are able to say about what they wish; speech is not directly affected. He can name objects, but he suffers from an inability to evaluate words, to grasp the idea of a conversation, and to hold it in memory. In reading, he understands the sense of certain words, but is unable to get the idea of the whole. The same is true in writing; he writes easily, but poorly; the grouping of the words is poor and the writing from dictation is inexact. He can copy well, but cannot explain a picture clearly — he becomes confused.

The trauma in these cases damaged the skull over the second parietal convolution. The injury went deeply into the substance of the brain. There was damage, but not destruction of the area in which visual images are laid down, and for that reason form sense and orientation were disturbed. This all indicates that it is not the pictures themselves, localized in the cortex, that were destroyed, but the connection between the visual pictures. Lesions of the second parietal convolution also cause apraxia — a loss of tactile ideas, and since general ideation depends on an association of visual, tactile and sometimes acoustic impressions, these lesions produce a disturbance in connecting up visual and tactile pictures — and from this results the defective logic in grasp of visual, auditory and tactile images.

The important thing which Head has developed in his sematic aphasia has nothing to do with aphasia. He localizes the process of combining pictures for purposes of logical thinking. This does not mean that the entire thought process is dependent on the parieto-occipital association zone; it is probable that this is a substation only.

As already stated, Head's work is purely clinical and lacks an adequate pathologic basis; nevertheless, there is plenty of evidence that Head, in spite of his theoretical considerations, merely confirms the views of the localizationists. Unfortunately, instead of clarifying the field, he has added to the chaos.

Following this critical summary of Head's work, Henschen discusses the various schools of aphasia, emphasizing the position of the localizationists who accept the four primary centers — the third frontal for aphemia, the first temporal for word deafness, angular gyrus for word blindness, and the second frontal for agraphia. Among them are a special group, the extremists, who carry the localization principle to its logical conclusions. They prophesy that, in the future, aphasia will be divided into countless forms, with countless localizations. Corresponding to this on the anatomic side, they promise a further subdivision of the Brodmann-Vogt zones into many smaller zones. Jendrassik demands a localization of individual words in individual cells; accepting the four primary centers, he demands others for special functions — for notes, for figures, for nouns and for verbs.

Henschen himself believes that the present chaotic state of the aphasia problem is due to faulty approach and faulty methods. He insists on facts—facts to begin with, and facts to continue with. He points out that the whole subject was at a standstill until certain facts were learned regarding the localization, organization and extent of the sensory zones of the cortex. The discovery of these zones (visual center by Henschen 1892; auditory center by Flechsig and also by Henschen 1894 to 1908) permitted the fundamental differentiation of physiologic fields and psychic fields. The more factual material he has studied, the more it has seemed necessary to divide anatomic zones and centers ad infinitum. "I have not yet," he says, "reached the point of an atomistic division of the cortex—only a cellular division." For the future he says, "Where the facts stop, the conclusions must stop and await further facts."

Henschen feels that the main result of his years of study of aphasia has been the proof that just as there are small physiologic cortical centers of specific structure and function, for vision and hearing, so also there are small, almost minimal centers, of specific structure, which subserve psychic functions.

SELLING, Portland, Ore.

MICROGLIA, ITS ORIGIN, FUNCTION, AND RELATION TO OTHER GLIA ELEMENTS. W. M. PRUIJS, Ztschr. f. d. ges. Neurol. u. Psychiat. **108**:298 (April) 1927.

Cajal conceived the nervous system as being made up of three elements: (1) the first element, the nerve cells; (2) the second element, the neuroglia; (3) the third element, the adendritic cells. Hortega, by means of his silver carbonate method, discovered that many of Cajal's adendritic cells contained processes, and that these cells from a morphologic and microchemical viewpoint, differed from neuroglia. Hortega named these cells "microglia" because they are smaller than the neuroglia and in contradistinction to the "macroglia" or neuroglia cells. Since he assumed them to be of mesodermal origin he called them mesoglia. Hortega's third element, however, did not correspond exactly to the third element of Cajal because the latter contained many cells called oligodendroglia which were first described by Robertson in 1900. In 1921, Hortega succeeded in staining these "microglia" cells and concluded that Cajal's third element consisted of microglia and oligodendroglia. Metz and Spatz believe the microglia is not mesodermal but ectodermal, and since "third element" is therefore a misnomer, they call these cells Hortega cells. The microglia is most abundant in the gray matter of the brain. The processes spread out in three dimensions so that it is impossible to get a microglia cell with all its processes in one photograph. Often a microglia cell lies at the base of a pyramidal cell and surrounds the cell body with its processes. They are common around blood vessels but they do not contain sucker feet.

Pruijs is concerned with three problems regarding the microglia: (1) the separation or delimitation of the microglia from oligodendroglia; (2) the origin of the microglia; (3) their pathologic degeneration forms. One important difference between microglia and oligodendroglia is that they are made visible by different procedures. Morphologically the two cell types are different. Oligodendroglia has a cylindric, eccentrically situated nucleus with small, fine granular protoplasm and fine threadlike processes which have a swelling at their extremities and are similar in structure to the protoplasm. Microglia, on the other hand, has a triangular nucleus, with less sharp differentiation between nucleus and cytoplasm, and with broader, more numerous processes. Both types are closely connected with nerve cells. The microglia nucleus is long and rodlike in contrast to the cylindrical nucleus of the oligodendroglia. The protoplasm is coarsely granular and has the same dark appearance of the nucleus, while the protoplasm of oligodendroglia stands out in sharp contrast to the nucleus as it is finely granular and hard to differentiate from its surroundings. The microglia processes branch off at right angles and end in fine prolongations, while those of oligondendroglia end in various swellings. Oligodendroglia lies in rows both in white and gray matter, but more pronouncedly so in the white matter. While microglia and oligodendroglia differ definitely in morphologic characteristics, Pruijs says that intermediary types or transitional types between the two occur showing staining characteristics common to both cell types.

Pruijs investigated the origin of microglia cells in rabbits. He concluded that microglia cells are never present in the new-born rabbit. Instead there appear at this time rod-like, club-shaped and wedge-shaped bodies which Pruijs takes to be the nuclei of microglia cells on account of their staining properties. In places the resemblance to microglia nuclei is very striking. The white matter in this stage is filled with small rods which are radially arranged in the gray matter and directed toward the pia. Later they lose their radial arrangement and snuggle close to the nerve cells. In this later stage also, having lost their radial arrangement, they first show their processes. These cells occur near the ependyma in great numbers, and protoplasmic processes connect these in the ependymal region with those cells in the white matter. From this process and from the loss of their radial arrangement Pruijs concludes that these bodies migrate. The argument against their migration from the pia is that the connecting processes are directed from the

ependymal area toward the cortex. These nuclear forms, moreover, are never found in the pia or in the vessels. Only in the ependyma are such forms seen, and Pruijs holds for the ectodermal origin of microglia cells, migration occurring via protoplasmic processes toward the cortex and the pia.

Microglia cells are closely concerned with metabolic functions in the nervous system. Hortega described their swelling in toxic-infectious conditions: meningitis, meningo-encephalitis, uremia, general paralysis and other diseases. The microglia cells swell, lose their processes, become pale and round, fill with waste products and degenerate finally into compound granular cells which stain for fat. Each element of the microglia changes so much as to become a caricature of the normal. The protoplasm becomes paler, the processes swell. It is at once clear from this that the rod cells are not bipolar microglia cells. An interesting fact also is that in general paralysis many microglia elements contain iron, especially in the corpus striatum and cornu ammonis. In areas of softening also they contain iron pigment. Metz and Spatz, who first disclosed this fact, concluded that microglia had to do with the transportation of iron and that without doubt microglia played a phagocytic function. Pruijs attempted to show experimentally that microglia cells have to do with metabolic functions in the nervous system. He found definite changes in the microglia of a dead rabbit into the carotid arteries of which coagulated blood had been injected. The cells were pale, the protoplasm swollen, the finer processes lost; the changes were most marked in the cornu ammonis. Similar changes were found in an animal which had been bled to death.

Microglia in pathologic conditions was studied in animals which had been injected with rabies virus. In these animals, the microglia was more readily visible, with broad, darkly staining processes. They were most markedly degenerated around blood vessels, and appeared visible in the lamina zonalis, a locus where they are ordinarily very hard to demonstrate. Similar observations were present in the cornu ammonis, except that they were more marked, the microglia cells degenerating into compound granular cells. Pruijs concluded that the microglia cells take up all the waste products in the central nervous system and transport them to the blood vessels.

Hortega takes for granted the fact that the microglia are the phagocytic cells. These are the only glia cells with phagocytic function. Pruijs, however, in rabbits and mice injected with zoster virus, shows that the phagocyting function in neuronophagia is not the work of only the microglia. He shows by photographs that the active invasion of the nerve cells is carried out by the oligodendroglia, whereas the carting away of the debris is the function of microglia cells.

ALPERS, Philadelphia.

COMPARATIVE MEASUREMENTS OF THE ALLOCORTEX IN ANIMALS AND IN MAN. STELLA ROSE, J. f. Psychol. u. Neurol. **34**:250, 1927.

The object of this investigation was to compare the surface measurements of particular cortical regions in the allocortex of man and of various animals. Genetically, the allocortex consists of three regions: (1) cortex semiparietinus sive striatalis; (2) cortex totoparietinus schizoprotoptychos; (3) cortex totoparietinus holoprotoptychos bistratificatus. The following regions of the cortex striatalis were measured: regio prepyriformis, tuberculum olfactorium and regio diagonalis; the cortex totoparietinus schizoprotoptychos, consisting principally of the regio entorhinalis, throughout its entire extent; the cornu ammonis, which is included in the cortex totoparietinus holoprotoptychos. In addition, the bulbus olfactorius was also measured. The animals studied were only those in which the various components of the allocortex are well known: (*a*) Marsupialia *(Didelphys azarae);* (*b*) Insectivora *(Erinaceus europaeus);* (*c*) Carnivora *(Canis domesticus);* (*d*) Prosimiae *(Lemur catta);* (*e*) Primates *(Cynocephalus hamadryas, Troglodytes niger, Homo sapiens).*

Of mammals, the dog has by far the largest bulbus olfactorus (457 sq. mm.); this harmonizes well with the extraordinarily well developed olfactory function in this animal. Strikingly, the hedgehog with its unusually small brain has an olfactory bulb more than twice the size of that in the chimpanzee or baboon and 25 per cent larger than in man. The contrast is still more striking in the didelphys as compared with the primates. These facts would seem to indicate that the receptive surface for olfactory impressions is smallest in the primates. The olfactory bulb as compared with the entire cortex is considerably larger in lower mammals than in primates.

The region prepyriformis is largest in the dog but almost half the size of the bulbus olfactorius. In the didelphys as well as in the hedgehog, the bulbus olfactorius is also more than twice the size of the regio prepyriformis; not until the primates are reached is the ratio of the surface of the bulbus olfactorius to that of the regio prepyriformis almost 1:1.

The tuberculum olfactorium (lobus parofactorius in lower mammals) in primates is the homolog of the substantia perforata anterior exclusive of the regio diagonalis. The size of the tuberculum olfactorium in the animals examined was: in *Didelphys azarae,* 28 sq. mm.; in *Erinaceus europaeus,* 24 sq. mm.; in *Canis domesticus,* 57 sq. mm.; in *Lemur catta,* 20 sq. mm.; in the baboon, 54 sq. mm.; in the chimpanzee, 40 sq. mm. and in man, 100 sq. mm. The size of the regio diagonalis was: in the *Didelphys azarae,* 12 sq. mm.; in *Erinaceus europaeus,* 6 sq. mm.; in *Canis domesticus,* 38 sq. mm.; in *Lemur catta,* 10 sq. mm.; in the baboon, 28 sq. mm.; in the chimpanzee, 29 sq. mm.; in man, 46 sq. mm.

Considering the sensory olfactory epithelium as an olfactory station of the first order, the bulbus olfactorius could be regarded as an olfactory station of the second order, whereas the entire cortex semiparietinus would be an olfactory station of this order. The size of the entire cortex semiparietinus was: in the *Didelphys azarae,* 155 sq. mm.; in *Erinaceus europaeus,* 118 sq. mm.; in *Canis domesticus,* 446 sq. mm.; in *Lemur catta,* 116 sq mm.; in the baboon, 138 sq. mm.; in the chimpanzee, 138 sq. mm. and in man, 290 sq. mm. The ratio of the size of the surface of the bulbus olfactorius to that of the cortex semiparietinus in lower mammals is almost 1:1; in half-apes (animals on the borderline between macrosomatic and microsomatic animals), this relationship becomes 1:2 In primates, the surface of the cortex semiparietinus exceeds that of the bulbus olfactorious, and in man it is almost four times as large.

The size of the cornu ammonis was: in *Didelphys azarae,* 85 sq. mm.; in *Erinaceus europaeus,* 45 sq. mm.; in *Canis domesticus,* 220 sq. mm.; in *Lemur catta,* 146 sq. mm.; in the baboon, 274 sq. mm.; in the chimpanzee, 270 sq. mm.; in man, 750 sq. mm. The surface of this structure is therefore largest in man; it is also relatively large in other primates but is actually smaller than in man. Whereas in macrosomatic animals the bulbus olfactorius is twice the size of the cornu ammonis, this relationship is reversed in microsomatic animals. In monkeys, the cornu ammonis is more than six times as large and in man more than ten times as large as the bulbus olfactorius.

There is a similar relationship in the entorhinal region; the surface of the latter is largest in man. Whereas in lower mammals the bulbus olfactorius is always considerably larger than the regio entorhinalis, this relationship is just the opposite in primates, i.e., the size of the regio entorhinalis exceeds that of the bulbus olfactorius by five times in the baboon, by seven times in the chimpanzee and by ten times in man.

KESCHNER, New York.

SOME NEUROLOGIC COMPLICATIONS OF THE EAR, NOSE AND THROAT. THEODORE H. WEISENBURG, Arch. Otolaryng. **5**:469 (June) 1927.

Weisenburg discusses briefly the most important nervous complications of the ear, nose and throat. Optic atrophy may be caused by swelling of the nerves as a result of osteitis, periostitis or swelling of the soft parts through extension of the inflammation. In some cases, sinusitis cannot be demonstrated.

yet an operation cures the condition; these cases may be due to a toxic influence. Retrobulbar optic atrophy is more common than optic neuritis. Primary optic atrophy never occurs from disease of the sinuses. Neurologists are agreed that choked disk is caused by increase of intracranial pressure; therefore it cannot be caused by ethmoidal or sphenoidal lesions. Optic neuritis with 2 or 3 diopters of swelling may be seen in postethmoidal and sphenoidal lesions, but never a frank choked disk. Weisenburg advises against operations on the sinus before a thorough general examination is made. He has seen operations on the sinus performed in cases of tabes dorsalis and of tumor of the brain; and he emphasizes the necessity of a careful neurologic examination before undertaking a hurried operation on the sinuses because of the presence of choked disk.

There are three theories in regard to pain in the face not due to involvement of the fifth nerve. 1. It is due to involvement of the ninth nerve, inflammation of which will give pain in the lower part of the face, tongue and throat. 2. It is due to involvement of the sphenopalatine ganglion. In most of Weisenburg's cases the results of treatment have been disappointing; while cocainization has temporarily alleviated the pain, alcoholic injection has not. He thinks that all these cases are not due to sphenoidal sinusitis irritating the nerves central to the ganglion. He concludes, however, that there is "such a thing as nasopalatine pain as described by Sluder, but that this syndrome is uncertain." 3. The pain may be carried by the sympathetic nerve. The theory of André Thomas that there may be sensory fibers coming from the posterior ganglions through the sympathetic nerves to the periphery may be correct, but it has not been proved. Weisenburg warns against indiscriminate operations on the sympathetic nerves at present. The pains may also be of psychogenic origin.

Inflammatory Processes: Intracranial complications occur more frequently after ear disease than after sinusitis. Most abscesses of the brain follow chronic otitis. Abscess of the brain from middle ear disease occurs more frequently in the temporal lobe (70 per cent) than in the cerebellum (30 per cent).

Meningitis: Weisenburg emphasizes the difference betwen meningismus and meningitis, and calls attention to the fact that the organisms in meningitis may not be found at the first examination.

Abscess of the Brain: Acute cases are more difficult to diagnose because of lack of advance in the symptoms. In chronic cases, abscess of the temporosphenoidal lobe offers the greatest diagnostic difficulty. Acute abscesses are more likely to occur in the cerebellum. Disturbances of speech, visual hallucinations and hemianopic vision may be found. This is also observed in frontal lesions. Frontal lobe lesions are usually not recognized until the adjacent motor area is involved, causing hemiplegia and jacksonian convulsions on the opposite side. Pressure phenomena may not be observed. The vestibular tests are of value when interpreted for known pathways. The labyrinth has an influence on the tonus of the muscles.

Vertigo from toxic disease and epilepsy and of functional origin is discussed. Cases of vertigo of toxic origin due to disease of the tonsils, teeth and colon are reported. The toxemia may also involve the cochlear branch. Syphilis is a common source of neuritis of the eighth nerve. It is difficult to make a differential diagnosis between aural vertigo and minor epilepsy, both types may occur during sleep. Functional vertigo is frequently observed in neurasthenic patients and in traumatic neuroses.

During the war hysterical deafness and aphonia were common. Hyperacuity of hearing may also occur. Hyperosmia or dysfunction of smell is not infrequently an hysterical phenomenon. Throat neurosis, such as sudden swallowing, constant coughing, clearing of the throat, may be observed in hysterical or neurotic patients.

HUNTER, Philadelphia.

MEGALENCEPHALY AS A BASIS OF IDIOCY. K. PETER and K. SCHLÜTER, Ztschr. f. d. ges. Neurol. u. Psychiat. **108**:21 (April) 1927.

Marburg first applied the term "hypertrophy" to brains that showed a generalized increase in all their elements. In addition to hypertrophy he described hyperplasia. Virchow differentiated true from interstitial hyperplasia according as all elements or only the interstitial elements were increased. Virchow believed the former was physiologic and the latter pathologic. In addition, he described localized primary diffuse glioses which were hyperplasias but must be looked on as neoplasms. Fletcher later changed the term hyperplasia to megalencephaly, meaning by this a symmetrical enlargement of the entire brain. Many cases of megalencephaly have been reported both in normal people and in idiots. Megalencephaly in epileptic persons and idiots has been described by Virchow, Walsem, Anton, Fletcher, Hausemann, Obersteiner and others. All these cases showed practically similar observations: enlargement of the entire brain, enlargement of the cells, and increase in all elements of the brain. Tsiminakis described an interesting case of a boy, aged 8, with megalencephaly; the boy had keen intelligence and no psychic symptoms, but severe attacks of headache and vomiting. The brains in these cases weighed from 2,000 to 2,200 Gm.

Peter and Schlüter describe the case of a boy, aged 3½, who had developed very little from the time of birth. He had not been able to walk, stand, talk or sit up. He could not perform any coordinated movements. At 6 months he had had a cranial circumference of 45 cm. and at 3½ years of 55 cm. The head was very heavy. The right extremities were less well developed than the left. Twitchings and athetosic movements occurred, and, later, epileptic convulsions recurred from once to forty times a day. After two and one-half years the patient developed irregular fever, lost weight, and gradually became worse until the time of death. The clinical diagnosis was organic brain disease: hydrocephalus internus?

Necropsy revealed thin bones in the skull and closed fontanels. The convolutions of the brain were normal; some were broad, especially in the left temporal lobe. The frontal section showed a strikingly wide cortex without enlargement of the ventricles and without the formation of a tumor. The callosum and commissures were relatively very small. The cerebellum was normal and corresponded in size to that of an adult. The cerebellum weighed 200 Gm.: the brain stem, 20 Gm., and the cerebrum, 1,770 Gm. The brain stem was much too small in relation to the cerebrum and the cerebellum. Histologically, the most important observation was generalized increase in the width of the cortex, both architectonically and histologically. Cell measurements showed a definite increase over the normal. The Betz cells measured 115 by 69 microns in contrast to 80 by 110 for the normal cell. The cerebellum was much too large in relation to the cerebrum and the Purkinje cells measured 50.5 as against 45.2 microns for the normal. The basal ganglia showed both an absolute and a relative increase in size. In marked contrast, however, to the increase in width of the cortex was the fact that the white matter was smaller than normal; so also was the corpus callosum. There was present a megalencephaly with hypertrophy and hyperplasia of the cerebrum, cerebellum and subcortical gray masses and with decreased white matter and commissural connections. The pia was thickened in parts and infiltrated with histiocytes and lymphocytes. In places the vessels showed endarteritic thickenings. There was striking diffuse proliferation of protoplasmic glia in the cortex with a tendency to the formation of giant glia cells. This was more marked in some places than in others. In places the glia collected in small groups such as are seen in encephalitis; apparently they consisted of Hortega glia. Elsewhere the Hortega glia was not increased. In places, granulomas consisting of collections of lymphocytes were present. Small perivascular infiltrations were also present. The Purkinje cells in the cerebellum showed degenerative

changes similar to those described in juvenile general paralysis, with double nuclei and loss of cell contour. Bielschowsky has described this in psychoses and idiocy; Ranke and Schröder look on such cell anomalies as a stigma of degeneration.

ALPERS, Philadelphia.

PICK'S DISEASE. CARL SCHNEIDER, Monatschr. f. Psychiat. u. Neurol. **65**:220 (June) 1927.

The author reports two cases of Pick's disease, with careful clinical and pathologic studies. He reviews the literature of the subject and attempts an adequate formulation of the disease picture: clinical course, psychopathology, gross and microscopic pathology, and the differential diagnosis from other types of progressive dementia of advanced years—Alzheimer's disease, arteriosclerotic and senile dementia. Pick's disease may develop at any time after 40. It is more frequent in women. The duration is from three to twelve years, and the outcome is always fatal. The etiology is wholly unknown. In the development of symptoms three stages are recognized. The first stage begins with a compulsive activity, restlessness and lack of inhibition. The patients are constantly on the go and are childish and silly; they joke and pun, are inattentive, and hard to hold to a given task. Often they lose their moral hold—lie, steal, pile up debts and are sexually unstable. Often these actions depend on sudden unconsidered impulses. On the emotional side, marked depressions are uncommon; usually the patients are dull, indifferent and without interest, and the affects have a superficial character. This, and the absence of delusions, hallucinations and confabulation makes the characteristic picture at this stage.

The second stage shows a progressive development of the dementia which was indicated in the first stage. This dementia is characterized by an involvement of the higher psychic functions (finer combinations and judgment), whereas the simpler, more elementary functions of attention and memory are relatively intact. The few focal symptoms which characterize the disease develop at this time. The cases with predominant frontal lobe localization show lack of initiative, while the cases of the temporal lobe show a more or less marked aphasic picture, especially of the amnestic aphasic type. Characteristic of this stage are what Schneider calls "standing symptoms"—"stehende Symptome." "I use this new term purposely," he says, "because these complex symptoms, lasting year after year in the same form, are neither verbigeration nor stereotypy." They are not focal, occurring in the frontal as well as in the temporal lobe cases. These "standing symptoms" may consist of phrases, repeated monotonously, or of gestures or of mimicry. One patient repeated over and over, "Du bist verrückt," another, "ein tellerchen Brei"; other patients whine or bark, stamp or cry—over and over, in the same way. In still others, there is a routine of monotonous song, laughter and grimaces.

Hallucinations, delusions and, except in rare instances, confabulations, are still absent; the second stage gradually goes over into the third or terminal stage. Here one finds progressive dementia and extreme limitation—atrophy—of speech. Even here, however, one can still recognize the difference in involvement of higher psychic functions as compared to the simpler, primary functions. The patients become worse steadily and more or less rapidly; they lose weight, contractures develop, and death comes either from the disease itself, or from pneumonia or other intercurrent infection.

Following the clinical description is a careful pathologic report, both gross and microscopic, of his own two cases and a discussion of previous cases. Grossly the brains show regional atrophy, localized especially in the frontal pole (frontal cases) and in the temporal zone, especially the gyrus fusiformis (temporal cases). The essence of the picture, as summarized by Spatz, is as follows: Lack of arteriosclerotic changes in the vessels supplying the atrophic zones, lack of characteristic arteriosclerotic changes in the brain tissue itself; absence of senile plaques and fibrillar changes; absence of intensive tissue

destruction. On the positive side, loss of nerve cells, especially in the three upper layers of certain cortical areas, the result of "an atrophic process in the narrower sense." In addition, swelling of nerve cells, and rather marked involvement of the protoplasmic glia.

In summary, Schneider says that Pick's disease is usually unrecognized. He believes that the clinical picture, the course, and the pathologic picture taken together, are sufficiently characteristic to justify its being considered a disease entity—a type of dementia to be separated off from the previously accepted dementias of advanced years—Alzheimer's disease, arteriosclerotic dementia and senile dementia.

SELLING, Portland, Ore.

LOCAL SPECIFIC THERAPY OF EXPERIMENTAL PNEUMOCOCCAL MENINGITIS. I. EXPERIMENTAL PNEUMOCOCCAL MENINGITIS IN RABBITS. II. THE PRODUCTION, PATHOLOGY AND TREATMENT OF TYPE I PNEUMOCOCCAL MENINGITIS IN DOGS. FRED W. STEWART, J. Exper. Med. **46**:391 (Sept.) 1927.

These studies of experimental pneumococcal meningitis from the Laboratories of the Rockefeller Institute for Medical Research should be read by all who are interested in the treatment of this disease, which is nearly always fatal in human cases. The author's conclusions in regard to the rabbit experiments are: (1) Fatal type I pneumococcal meningitis may be produced in rabbits by intracisternal injection of pneumococci. (2) When organisms are of high virulence, the rabbit does not tend to localize them in the meninges, but an early septicemic process results. Death is septicemic rather than meningeal. (3) In such instances very little cellular reaction occurs in the meninges. (4) Active or passive immunization previous to intracisternal infection inhibits partially the septicemia and permits the development of reactional processes in the meninges. (5) The immunization likewise retards the meningeal disease, but multiplicity of factors prevents us from stating precisely to what this retardation is due. It is not correlated with the presence of agglutinins in the spinal fluid at the time of infection. (6) The rapidity of production of meningitis is influenced by the phase of growth of the culture used, and likewise by the growth activity of that culture. (7) To some extent in the partially immune rabbit the meningeal spaces constitute a relatively nonimmune reservoir, constantly feeding the blood stream and breaking down systemic resistance. (8) Intrathecal serum treatment causes rapid agglutination and phagocytosis of pneumococci, and has very rarely, possibly, resulted in cure. Essentially no phagocytosis occurs in the absence of immune serum. (9) Phagocyted pneumococci stained supravitally take up the neutral red stain and are therefore probably injured. (10) The treatment employed subsequent to infection only slightly prolongs life in the majority of cases. It does retard septicemia. (11) The treatment improves the cellular reactional processes in the meninges. (12) A study of the pathology of rabbit pneumococcal meningitis shows that the location of pneumococci precludes complete contact with serum introduced intrathecally, and that these locations provide isolated foci, from which organisms may reinfect the meningeal spaces as rapidly as they are removed by lavage or injections of antibody. (13) In recovered rabbits postmeningeal symptoms, weakness, ataxia, nystagmus and paralyses arise. (14) It is my opinion that there is some objective evidence of benefit of serum therapy. The rabbit is too susceptible, however, and conditions too artificial to admit of definite conclusions. (15) Rough type I pneumococci introduced in large quantity cisternally may kill and may be recovered twenty-four hours after infection, from spinal fluids. In a series of eleven passages, no reversion to smooth type occurred. In all animals injected with rough forms, transient bacteremia resulted.

Concerning the experiments with dogs the author concludes: (1) Extensive acute, fibrinopurulent meningitis may be produced in dogs by the intracisternal injection of virulent type I pneumococci. (2) Given an equal number of

virulent infecting organisms, the rate of establishment of infection depends upon the phase of growth and the quantitative growth per hundred cubic centimeters of culture plus an uncontrollable individual factor in the animal. (3) The pathology of pneumococcal meningitis is discussed. It closely resembles the similar disease in man. (4) Systematic lavage and treatment with optochin serum mixtures by the method of quadruple puncture, as already described , have resulted in cures of type I pneumococcal meningitis in dogs. (5) The important factor in obtaining cures is to bring all regions of the meninges into frequent contact with the therapeutic agent. (6) In the absence of such contact, incomplete sterilization results and "reinfection" is almost inevitable. (7) Protocols show the necessity of repeated negative cisternal fluids, both on smear and on culture, before sterilization can be assured. (8) Recovered dogs subjected to meningeal reinfection show some degree of resistance.

FREMONT-SMITH, Boston.

UNILATERAL HYPERHYDROSIS OF THE FACE FOLLOWING TRAUMA AND PROVOKED BY TASTE AND HEAT. A. SOUQUES, Nev. neurol. **12**:145, 1927.

The syndrome of the auriculotemporal nerve, described in 1923, is characterized essentially by flushing and sweating of the cheek following gustatory stimuli and is caused by irritation of the auriculotemporal nerve in the parotid region. This irritation, however, remains latent and the sympathetic phenomena are elicited only by eating. The flushing is limited to the cheek and the sweating to a triangular area with its base along the anterior margin of the ear and its apex at the labial commissure. The glossopharyngeal nerve is the centripetal pathway and the auriculotemporal nerve an efferent pathway. In 1920, the patient described had fallen downstairs, on to his left side and had received a wound in the left side of the forehead with a fracture of the left humerus. The patient was conscious, and was able to go home alone. The wound of the eye was healed in about ten days. Nine months later there was still some difficulty with the arm and the scar remained visible. Two or three days after the accident, localized sweating occurred on the left side of the face and persisted, coming on in crises during eating and at night. The sweating was sometimes profuse, lasting about twenty minutes during the day and a little longer at night. At the end of the crisis the patient felt great fatigue and a desire for sleep. On examination six minutes after the beginning of a meal, localized sweating appeared on the left side of the forehead and chin. There were no vasodilator phenomena in the cheek. Following the injection of pilocarpine the sweating was pronounced over the scalp and upper third of the neck on the left side, later extending to the right side. As the sweating spread, the left side was affected more intensely than the right. There was marked salivation, tachycardia and shivering. The most effective stimulus seemed to be acid and heat.

While reflex hyperhydrosis of the face is rare, unilateral hyperhydrosis caused by excitation of the neural centers is rather common. In two cases of syringomyelia, involving the cervical region, there was marked sweating on one side, coming on in the first case when the patient was walking and, in the second case, without known cause. In one of these instances hyperhydrosis was the first symptom. In these cases the injection of pilocarpine is usually, but not always, followed by a large increase in sweating on the affected side. Crises are the rule. In another case of spinal lesion, the sweating affected one hand and forearm and the pains were worse at this period. Occasionally the topography of the sweating will indicate the level of the lesion as in a case in which a patient suffered a fracture dislocation of the vertebrae with paraplegia; there was a sharp demarcation between the dry area below the level of the lesion and the moist area above. In cases of hemihydrosis of cerebral origin the causative lesion has not been localized. The condition is even seen in parkinsonism. There are sometimes other crises of

headache, vertigo or convulsions which do not give any useful indication. Neither the physiologist nor the pathologist has yet discovered their location, although such centers have been postulated in the cerebral cortex, the basal ganglia, the midbrain and the medulla.

FREEMAN, Washington, D. C.

THE SUGAR CONTENT OF THE CEREBROSPINAL FLUID IN EPIDEMIC ENCEPHALITIS AND OTHER DISEASES OF THE CENTRAL NERVOUS SYSTEM. C. J. MUNCH-PETERSEN and KNUD WINTHER, Acta psychiat. et neurol. **1**:188, 1926.

Using the method of Hagedorn-Norman-Jensen, the authors investigated the amount of sugar in the blood and cerebrospinal fluid in twenty-nine patients with epidemic encephalitis, five with cerebral tumor (only one of which was verified) three with epilepsy, six with cerebral softening, two with cerebral arteriosclerosis, two with paralysis agitans, twelve with cerebrospinal syphilis, three with tuberculous meningitis, and one each with dementia praecox, hematomyelia, polyneuritis, multiple sclerosis, tumor of the spinal cord and aseptic meningitis. The sugar content of the cerebrospinal fluid was studied also in eight healthy young persons, and after death in one case of general paralysis and one of multiple sclerosis. The authors found a relative increase in the sugar content of the cerebrospinal fluid over that of the blood in the acute but not in the chronic forms of encephalitis; the examination had no value in deciding whether in the four patients with tumor of the brain in whom the diagnosis was doubtful, the condition was neoplasm or epidemic encephalitis. The one patient in whom the tumor of the brain was verified showed an increase in the sugar content of the fluid; the authors attribute this to the location of the lesion—in the corpus callosum. Two of the epileptic patients showed normal spinal fluid sugar; in the third case it was increased. The authors think, however, that the sugar content of the fluid is increased immediately after a seizure; the examination may serve, therefore, to differentiate a hysterical from an epileptic convulsion. Sugar was increased in the patient with paralysis agitans and in the one with tumor of the spinal cord. In the latter, the sugar content of the blood was normal, and they attribute the increase in the cerebrospinal sugar to meningeal compression. Sugar is decreased in neurosyphilis, the decrease being in inverse ratio to the number of cells. In tuberculous meningitis there is an increase in the sugar content of the blood and a decrease in that of the cerebrospinal fluid. In aseptic meningitis and multiple sclerosis, the fluid sugar was diminished. In the other conditions it was normal except in a patient with cerebral softening with a thalamic syndrome who showed an increase in the fluid sugar content. Both of the patients examined at postmortem showed an increased sugar content of the cerebrospinal fluid.

The authors conclude that a relative increase in the sugar content of the cerebrospinal fluid is not a diagnostic sign of epidemic encephalitis but that it is of service in distinguishing the acute stage of this disease from diseases such as the meningitides that show a decreased fluid sugar. Examination of the sugar content of the cerebrospinal fluid is of service in distinguishing the meningitides from meningismus, and epileptic convulsions from hysterical convulsions. It has a prognostic value in meningitis for it begins to rise toward normal before any clinical improvement is noted in the patient.

PEARSON, Philadelphia.

CHRONIC TEMPOROSPHENOIDAL ABSCESS: DISCOVERED DURING AN APPARENT ACUTE SUPPURATIVE OTITIS MEDIA: REPORT OF A CASE WITH POSTMORTEM OBSERVATIONS. EDWARD R. ROBERTS, Arch. Otolaryng. **6**:213 (Sept.) 1927.

This is the report of a case in which a patient suffered from an acute otitis media in the left ear. Paracentesis performed five days after the onset, on the occasion of her first visit to the physician (July 20), relieved the pain, improved the hearing, and apparently she was taking the normal course.

During the next week, she had four teeth extracted under gas anesthesia, three of them being definitely abscessed and the fourth devitalized. When she returned to the physician two weeks after the first visit, the ear had apparently recovered, the discharge now being small, but the patient showed evident signs of mental trouble and gave a history of great mental irritability. An internist then examined her thoroughly, but no physical signs, other than rambling conversation and a slight serous discharge from the left ear, were noted. The diagnosis of mental exhaustion due to loss of sleep, or toxic absorption, was considered. She was placed in a hospital. The white blood cells numbered 12,200. She had pain over the left forehead and eye, and talked incoherently. The following day a slight purulent discharge, without odor, appeared in the left auditory canal. It now developed from the history that the patient had had chronic otorrhea in the left ear for years, about which she had been exceedingly sensitive. Ophthalmic examination showed retinal veins dilated with a beginning optic neuritis. Roentgen-ray examination showed sclerotic mastoids. The spinal fluid contained 140 cells per cubic millimeter and was under pressure; no organisms were found. The pulse rate was from 80 to 84, and on one occasion 60; on August 4 there was some twitching of the left leg. The neurologist considered the possibilities of an abscess of the brain, localized encephalitis, or a right cerebellar disturbance. Slight spasticity of the right leg was noted. Exploratory operation of the left temporosphenoidal lobe was advised, but was refused. On August 7, a slight generalized convulsion of short duration was followed by vomiting for the first time, and the patient relapsed into semicoma. A divergent squint was noted. Convulsions became frequent and the family finally consented to operation. The temporosphenoidal lobe was exposed, but the patient died on the table. Autopsy showed a large nonencapsulated abscess containing thin gray pus, high up and well back in the left temporosphenoidal lobe.

The author notes concerning the previous general health: no recurrent headaches, no vomiting or convulsions until late in the disease, no slow pulse, and the temperature only slightly subnormal at intervals. The twitchings in the left leg were probably due to conical pressure catching the tracts, at intervals, on the left side before they have crossed or on the right side after the decussation.

HUNTER, Philadelphia.

THE MICROSCOPIC ANATOMY OF INFANTILE AMAUROTIC IDIOCY. ROY R. GRINKER, Arch. Path. **3**:768 (May) 1927.

The microscopic pathologic condition of the two cases of infantile amaurotic idiocy reported seems to demonstrate the successive stages in the progress of the disease process. Some of the cells were of normal size and were angular in form, and the processes were visible for a long distance. The Nissl bodies were well formed but hyperchromatic, and the neurofibrils were normal. The nucleus was markedly swollen, filling most of the cell, and its membrane was sharply defined and regular. The nucleolus was large and intensely blue. The author considers that these cells show the initial stage of the disease process. At a later stage, a golden green lipoid substance appeared between the Nissl bodies in the region of the axon hillock. This was limited at first to the inter-Nissl substance, but later it replaced the Nissl bodies and extended to fill the entire cell. When this occurred the nucleus was pushed toward the apical dendron, and the cell became swollen to two or three times the normal size. The lipoid was contained in a finely reticulated argentophilic network, with uniform nodal points. The neurofibrils were decreased in number, and those present were pushed toward the periphery of the cell. In many cells there was a perinuclear mass of chromatin, and in these the nucleus was relatively lightly stained and the nuclear membrane was indefinite. Those cells that did not show the perinuclear chromatin had a sharply defined nuclear membrane. In the

terminal stage the cells were huge, round, and had a thick membrane. The nucleus was at one pole. The cytoplasm was filled with fine basophilic and argentophilic granules, embedded in a background of golden pigment. A network did not remain and only a few neurofibrils were seen pressed against the cell periphery. A few cells in the cortex and many in the thalamus were undergoing neuronophagia.

From his study, the author concludes that the process consists in a gradual replacement of the cell substance by lipoid material. He made a differential study of these lipoids and found that they were mixtures of cholesterol, phosphatids and cerebrosids, but were atypical in that they were not completely soluble in any lipoid solvent. Neutral fat was found only in gitter cells and then in a small amount. In a similar study, Hurst found that these lipoids, resulting from other types of neuronic degeneration, were readily converted into neutral fat and only the lipochrome pigment of senile cell change is completely insoluble. Grinker suggests that the cells in amaurotic idiocy primarily are normal and that after a period of normal functioning they undergo a pathologic process similar in its slowness and ultimate lipoid product to senility; that is, the process is really one of precocious senility, an abiotrophy in the sense of Gowers. The retinas were examined also. There was a severe alteration of the ganglion cell layers, but the other layers were normal.

PEARSON, Philadelphia.

ENCEPHALITIS RESIDUALS ASSOCIATED WITH MEASLES. F. HUST, München. med. Wchnschr., vol. 96 (Jan. 21) 1927.

In the past few years much has been written on the sequels of measles. Hust followed four interesting cases within a short period. In the first case, a child, aged 8½, developed symptoms of encephalitis five days after the onset of measles. An examination of the spinal fluid showed a positive Nonne-Apelt reaction and eighteen cells. After a ten day period of delirium and mental confusion, the patient gradually recovered. The second patient was a child, aged 7½, who following a recovery from measles developed a severe polio-encephalomyelitis. Three months after the onset of the complicating disease, the patient had made an almost complete recovery. The third patient was a child, aged 2, who was taken ill suddenly with a high temperature and generalized clonic convulsions. A left hemiplegia developed rapidly within a few days. On the fourth day a measles rash appeared, which ran its usual course. The fourth patient was a boy aged 6, who at the time of the attack of measles was in a state of lethargy for three weeks. After a short time, he began to have attacks of what appeared to be narcolepsy; but because of the length of these attacks, which varied from fifteen minutes to several hours, the author doubted that this was a case of true narcolepsy. He does not come to any definite conclusion.

There is little question but that these four cases presented a picture of encephalitis associated with measles. It is strange that at times there appear to be epidemics of cerebral complications associated with certain diseases such as grip, herpes, mumps and other conditions. One writer in a period of seventeen months found thirty-four cases of encephalitis following vaccination. It would seem that these processes may produce a neurotropic change which activates an encephalitis rather than that there is a specific reaction for each of these acute infectious processes. The difficult question to answer is: Are the cerebral disorders due to a specific measles toxin, or is there a secondary infection, the measles simply having lowered the patient's general resistance? The former view has been generally accepted, although there is no proof that such is the case. It is the writer's contention that the measles is only an activator for some secondary neurotropic virus.

MOERSCH, Rochester, Minn.

TONIC EYE FITS ("OCULOGYRIC CRISES") IN CHRONIC EPIDEMIC ENCEPHALITIS. AUGUST WIMMER, Acta psychiat. et neurol. **1**:173, 1926.

Although paralysis of eye movements occurs frequently in epidemic encephalitis, the author has observed only five cases of spasmodic associated movements of the eyes, which he reports, among about 300 encephalitic patients. The ocular syndrome consists of spasmodic conjungate deviation of the eyeballs, most frequently vertically or vertically and laterally. During the spasm the patient is unable voluntarily to change the direction of his gaze, or, if he can do so, he can maintain the new direction for a short time only. The movement of the eyeballs is associated with blepharospasm in some cases. The duration of the attack varies from a few seconds to several hours, and the attack itself occurs most commonly in the afternoon or evening.

This ocular syndrome is a late manifestation of chronic epidemic encephalitis and occurs almost exclusively in patients who show parkinsonism. It is rarely the only spasmodic phenomenon presented by the patient, usually forming part of more generalized tonic fits. It may be associated with either isolated palsies of the external eye muscles or paresis of associated movements. In certain cases the spasms are accompanied by pain; in most cases there is a feeling of anxiety. In one of the author's patients, this anxiety took the form of imperative hallucinations urging the man to commit suicide. Most authors believe that this ocular syndrome results from disease of the neostriatum, possibly, as Bing and Schwartz think, as a release phenomenon due to the temporary cessation of the inhibitory impulses that pass from the neostriatum to the pallidum and substriatal ganglia. Wimmer, however, points out that in certain cases extrastriatal irritation may produce the syndrome. Despite the close connection of vestibular functions and ocular movements, there is no proof that the condition results from any disturbance of vestibular function, but their resemblance to tonic cerebellar fits and the fact that one of his patients had definite signs of cerebellar disease inclines him to the belief that, in some cases, disturbance of some function of the cerebellum may be the cause.

Although Marinesco and Radovici have pointed out the great resemblance of this phenomenon to hysteria, the author thinks that this likeness is due to encephalitic and hysterical diseases utilizing the same pathways to produce symptoms.

PEARSON, Philadelphia.

PAINLESS MEDULLARY TUMORS. LAPORTE, RISER and SOREL, Rev. neurol. **2**:164, 1927.

In the majority of cases, juxtamedullary tumors, intradural or extradural, provoke intense pain, which is maximal at the location of the growth. In certain cases also, pains above or below the compression in the medulla suggest sympathetic or cordonal involvement. Nevertheless, certain tumors of the spinal cord are painless throughout their whole course, although they have been detected more frequently of late owing to the use of iodized oil 40 per cent. Those who first reported such cases believed the absence of pain was due to the softness of the tumor, but this view is not well taken since the softest of vascular and plastic sarcomas sometimes give rise to atrocious pain. Several explanations of the painlessness are possible. The histologic character has something to do with it, the neurinomas being the least painful of neoplasms, even when they arise from the posterior roots. Infiltrating tumors, especially those that penetrate the roots and spread apart the nerve fascicles, are particularly painful. The relationship of the tumor to the roots is of prime importance. Providing the tumor is immobile, little pain is apt to be produced; but those which are attached to the dorsal roots or slide over the posterior columns or anterolateral aspects of the spinal cord are especially painful since they are so easily displaced by the movement of the cerebrospinal fluid. This is well shown in the case of tumors when air is injected into the dural sac.

When the tumor completely blocks the canal, pain is not produced; but with freely movable medullary tumors injections of air give rise to lightning pains in the peripheral distribution of the root to which the tumor is attached. Another factor making for painlessness is compression of the spinal cord, which may, in some instances, result in spontaneous cordotomy.

The authors present a case in which pain was not present at any time in the course, in which motor disturbances were severe, and in which pain was not even provoked by the injection of air by lumbar puncture. Iodized oil 40 per cent was arrested at the level of the eleventh thoracic vertebra; the tumor was removed, but the patient developed bedsores and died fifteen days later. There was moderate demyelinization in the long ascending and descending tracts.

FREEMAN, Washington, D. C.

THE EFFECTS OF EXTENSIVE LOSS OF MUSCLE ON THE DEVELOPMENT OF SPINAL GANGLIA IN AMBLYSTOMA. S. R. DETWILER, J. Exper. Zool. **48**:1 (July 5) 1927.

Experiments were carried out with the view of effecting considerable muscle loss with only slight skin loss. Partial excision of the sixth, seventh and eighth myotomes in *Amblystoma* at the tail-bud stage of development is followed by hypoplastic development of the corresponding spinal ganglia. An analysis of the data obtained from a quantitative study of skin loss, muscle loss, and spinal ganglion-cell loss in the present experiments and in former experiments involving lateral fusion of two individuals shows that approximately 60 per cent of the cellular reduction in the spinal ganglia is due to skin loss, and approximately 40 per cent is due to muscle loss. The 40 per cent attributed to muscle loss is taken as an index of the proportion of proprioceptive neurons normally present in the ganglia. Incomplete myotomectomy does not appear to have any effect on the final proliferation of motor neurons in the cord. In almost complete absence of musculature, the ventral roots are well developed. From former experiments in spinal cord transplantation, it became evident that the extent of cellular proliferation within different levels of the spinal cord depended more on position than on the functional demands of the peripheral field. The influences limiting cell proliferation appeared to be determined primarily from within the spinal cord. Hence there would not appear to be any reason why variations in the amount of muscle should directly affect the extent of cellular proliferation. Furthermore, the adjustment to increased muscle seems to be more directly accomplished by repeated division of the axons. It seems reasonable to suppose that when muscle is reduced there might easily be a corresponding reduction in the spread of collateral fibers rather than a reduction in the number of neuroblasts which develop in the longitudinal motor column.

WYMAN, Boston.

THE ARCHITECTONIC STRUCTURE OF THE OPTIC THALAMUS IN HALF-APES (LEMUR CATTA). J. L. PINES, J. f. Psychol. u. Neurol. **33**:31, 1927.

The object of this investigation was to obtain a precise topographic analysis and to study the cyto-architectonic and myelo-architectonic structure of the optic thalamus. The half-ape was selected because, as far as Pines could gather, a detailed description of this structure in this animal had never been given. The investigation included a study of the regions of the optic thalamus, its nuclei and cells with their grouping, size, shape, structure and staining qualities, and a study of the thalamic fibers as to number, direction and thickness. For purposes of comparative study, the optic thalamus of other mammals, especially of apes (*Cercopitheci*), was utilized.

The results may be summarized as follows: The pulvinar, the oral part of the upper portion of the lateral nucleus and its mesial portion (strictly

speaking, the classic principal nucleus, centre médian) are not as well developed in *Lemur catta* as in *Cercopithecus;* these are all regions closely associated with the forebrain. On the other hand, the ventral thalamic nucleus or the lower portion of the lateral nucleus, chiefly its middle part, the anterodorsal part, especially the principal anterior nucleus and certain parts of the mesial portion of the thalamus as well as the nucleus parataenialis (here may also be included the tenia thalami, habenula) are better developed in the lemur than in *Cercopithecus.* These areas are all to be regarded as end stations of the prelemniscal radiation and of the lenticular radiations (Forel's bundle, H) or as related to the remote olfactory neurons; a similar relationship may also be seen in the geniculate bodies.

KESCHNER, New York.

MICRURGICAL STUDIES ON THE CONTRACTILE VACUOLE OF AMOEBA DUBIA (SCHAEFFER): I. RELATION OF THE PHYSICAL STATE OF THE INTERNAL PROTOPLASM TO THE BEHAVIOR OF THE VACUOLE. II. MICROINJECTION OF DISTILLED WATER. RUTH B. HOWLAND and HERBERT POLLACK, J. Exper. Zool. **48**:441 (Aug. 5) 1927.

Studies were undertaken for the purpose of accumulating data on the behavior of the contractile vacuole in artificially varied endoplasmic environment. Mechanical support is essential for systole of the contractile vacuole (or vacuoles) of *Amoeba dubia.* This is normally afforded by a gelated region surrounding the vacuolar membrane. When the gelated region around a vacuole is made fluid experimentally, mechanical support for contraction is removed and the diastolic interval is lengthened. Contraction of the gelated region around the vacuole may be considered as supplying the force required for absolute contact of vacuolar and plasma membranes. The mechanical stimulation and injury of an ameba caused by the entrance and removal of a micropipet induces changes which result in delayed contraction and dilatation of the vacuole. In the largest percentage of cases the cytoplasm appears more fluid and the ameba temporarily assumes a limax form. The output of the vacuole is increased. After slow successive injections of small amounts of distilled water, having a p_H of from 6.6 to 6.8, the contraction rate may be accelerated. The vacuolar output shows a pronounced increase. Amebas injected in this manner generally do not assume a limax form until after several injections have been made. After the first violent disturbances produced by rapid injection of a large quantity of water, there follows a period of recovery during which there is evidence of great lack of stability in the state of the internal protoplasm. Partial contractions are frequent and the amebas usually assume a limax form. In these cases the diastolic interval of the vacuole is lengthened and the fluid output is tremendously increased.

WYMAN, Boston.

CONGENITAL SYPHILIS TO THE THIRD GENERATION. C. P. BONDURANT, Arch. Derm. & Syph. **15**:695 (June) 1927.

Two cases of syphilis reaching the third generation are reported. In the first case the mother, after infection, was pregnant eleven times with five miscarriages, three stillbirths, two deaths in infancy and one living child, who showed physical signs of congenital syphilis. This girl later married a nonsyphilitic man; all three children born of this union had positive blood Wassermann reactions and physical signs of congenital syphilis. The record of the second case is less complete, but this, too, seems an authentic instance of congenital syphilis in the third generation. The literature on the subject is reviewed, and the mechanism of transmission of syphilis to the offspring is considered. The author concludes that the infection cannot be effected by the spermatozoon but is entirely maternal in origin and that transmission of the

disease to the fetus takes place through the placenta, as a direct infection of the blood stream, which accounts for the early death of the fetus and the high mortality of congenitally syphilitic infants in the first month of life.

KUBITSCHEK, Philadelphia.

EXTRAPYRAMIDAL MOTOR DISTURBANCES IN DEMENTIA PRAECOX. PAUL J. REITER, Acta psychiat. et neurol. **1**:287, 1926.

The author reports ten patients who had dementia praecox with motor disturbances. In the first six patients, a toxic terminal condition occurred. Gastro-enteritis and fever and the signs of general toxicity were accompanied by myoclonic and choreoathetosic movements, parkinsonian-like tremors, hypertonicity, increased reflexes, contractures, convulsions and, in several instances, signs of disturbances of the pyramidal tract. Necropsy showed gastro-enteritis and inflammatory changes in the liver, spleen, kidney and mesenteric glands. Reiter considers the last three cases reported to be a special type of dementia praecox which he calls dementia praecox parkinsonoides. These patients have shown the signs of parkinsonism in addition to those of dementia praecox for several years. Case 7 appears to be a transition form between the acute and chronic types. He considers that these cases indicate that dementia praecox has an organic rather than a functional basis and that in these patients the etiologic agent, possibly of a toxi-infectious nature, has involved the basal ganglia as well as the cortex.

PEARSON, Philadelphia.

THE FORMATION OF CONTRACTILE VACUOLES IN AMOEBA PROTEUS. HOWARD CALVIN DAY, J. Morphol. **44**:363 (Sept. 5) 1927.

There is a considerable diversity of opinion in the recent literature concerning the question as to whether the contractile vacuole in protozoa is a permanent organelle or merely a temporary structure. The present study indicates that the contractile vacuole in *Ameba* is not a permanent structure and has no specific relation, morphologic or physiologic, to any localized area. The contractile vacuole arises from the fusion of other vacuoles. Those in turn owe their origin probably to the fusion and coalescence of ultramicroscopic droplets of soluble katabolic waste which may include water of osmosis. The vacuolar "wall" is a condensation membrane or gel disappearing with each contraction. Conductivity water increases the size, number, and rate of pulsation of vacuoles. Multivacuolated amebas have otherwise normal behavior and are extremely active—a fact which is difficult to correlate with the suggestion that vacuoles are supported in gelated areas.

WYMAN, Boston.

FEVER IN TERTIARY SYPHILIS. H. M. KORNS, Arch. Derm. & Syph. **15**:652 (June) 1927.

The author discusses the subject of syphilitic pyrexia, reviews the literature and reports a case for the purpose of illustrating that quotidian, remittent and intermittent fever may be the chief manifestation of tertiary syphilis. The case reported is of interest in that quotidian nocturnal fever, with infrequent chills, was the chief symptom and existed, for variable periods of time, for two years with resultant loss of weight and neurasthenic symptoms. Serologic studies both of the blood and of the spinal fluid were negative, and moderate enlargement of the liver and spleen was the only positive physical manifestation. Malta fever, malaria and tuberculosis were considered to be excluded; a diagnosis of tertiary syphilis was made largely on therapeutic test. Iodides and mercury were of little value, but arsphenamine quickly produced a marked modification of the febrile reaction, reduction in the size of the liver and spleen and a return to normal weight.

KUBITSCHEK, Philadelphia.

CHVOSTEK'S FACIALIS SIGN IN NEW-BORN INFANTS. FRANK E. STEVENSON, A. GRAEME MITCHELL and CARL A. KOCH, Am. J. Dis. Child. **34**:425 (Sept.) 1927.

The authors studied the occurrence of Chvostek's sign in new-born infants and found that it was uniformly present. While the infant was sleeping, the sign was always elicited; when the patient was awake, however, the reaction was sometimes negative; and if the infant was crying or restless the sign was not obtained. In the majority of infants the blood calcium determinations were within normal limits. In others, with but one exception, the amount of blood calcium was above the limit at which tetany usually occurs. A total of fifty-five infants were examined. Of these, electrical reactions were determined on fifteen, and in all instances were normal. The authors conclude that since Chvostek's facialis phenomenon is found in new-born infants without clinical serologic or electrical evidences of tetany, it cannot be regarded as a pathognomonic symptom of this condition in early infancy.

VONDERAHE, Cincinnati.

DIFFUSE TUMORS OF THE LEPTOMENINGES. CHARLES L. CONNOR and HARVEY CUSHING, Arch. Path. **3**:374 (March) 1927.

The authors report the pathologic observations in two cases diagnosed clinically as pseudotumor cerebri. A tumor was not found on gross examination, but microscopic examination showed a diffuse tumor of the meninges. The primary tumor in the first case was multiple and grew from the adventitial or perivascular sheaths of the cortical vessels. The authors considered it a true sarcomatosis (endotheliomatosis) of the meninges—a rare type of growth. The second tumor represented an invasion of the meninges by largely undifferentiated embryonic cells (medulloblasts). As these primitive cells tend to undergo a certain degree of differentiation and when properly stained show occasional neuroglia fibers, they would name this growth meningogliomatosis. Both tumors had their primary origin in the region of the flocculus—a favorite area for the origin of neoplastic lesions.

PEARSON, Philadelphia.

TREATMENT OF NEURO-SYPHILIS AND PARESIS WITH MALARIA. H. GOLDSMITH and R. ROCKWOOD, Am. J. Syph. **2**:165 (April) 1927.

The authors review the history of malarial therapy and report personal experience with a group of fourteen patients. Except for three cases of chronic general paralysis, these were all of the early benign type and the importance of selecting such types for treatment is emphasized. The results, estimated one year after treatment, were considered satisfactory; 57 per cent of the patients were working at their regular vocations; two had died during treatment. Severe secondary anemia and loss of weight developed in nearly all cases, but physical improvement rapidly followed administration of quinine. Practically no modification of the serologic study of the spinal fluid was found. The authors conclude that this is a practical method of treatment and can be carried out in open wards without danger of contagion to other patients by mosquitoes.

KUBITSCHEK, Philadelphia.

BINASAL HEMIANOPIA IN SYPHILITIC AFFECTIONS OF THE BASIS CEREBRI. ARMINIO SEGUINI, Riv. Oto-Neuro-Oftalmologica **4**:299, 1927.

Seguini reports three cases of binasal hemianopia in which syphilis was proved, and in two of the cases nearly complete recovery took place. In one of these, which was associated with tabes, the patient experienced complete blindness in the nasal field. In these cases the macula was always involved, and limitation for color was often more pronounced than for form. The author

believes that the condition in two cases was meningitis and in another gumma. The location of the process must be at the lateral angles of the chiasma. The conditions responsible for binasal hemianopia are vascular dilatations or aneurysms, tumors of the pituitary, or meningeal exudates. The condition of binasal hemianopia in advancing tabetic atrophy seems not to have been reported before, and the abolition of macular vision in both eyes seems to be unusual.

FREEMAN, Washington, D. C.

COMPARISON OF A VIRUS OBTAINED BY KOBAYASHI FROM CASES OF EPIDEMIC ENCEPHALITIS WITH THE VIRUS OF RABIES. E. V. COWDRY, J. Exper. Med. **45**:799 (May) 1927.

During an outbreak of a form of epidemic encephalitis in Japan, in 1924, Kobayashi isolated a "virus" from a single case. Cowdry, studying this virus at the Rockefeller Institute for Medical Research, concluded: "Since the symptoms produced in experimental animals by the encephalitic virus of Kobayashi and by the virus of rabies are similar, and are accompanied by lesions, which are indistinguishable, and since a cross immunity is demonstrable between the two viruses, the conclusion is advanced that the specimen of so-called encephalitis virus, isolated by Kobayashi, is in reality a specimen of rabic virus."

FREMONT-SMITH, Boston.

GENERAL PRINCIPLES, TECHNIC AND RESULTS OF NEW TREATMENT OF INFANTILE PARALYSIS. H. BORDIER, Acta Psychiat. et Neurol. **2**:1, 1927.

The method described in this article consists in the association of radiotherapy of the spinal cord and of diathermy of the parts involved with such electrotherapy of the atrophied muscles as may seem necessary. The combination is based on the fact that the lesion consists early of a diffuse meningomyelitis with edema, followed by the destructive action on the anterior horn cells. In a total of sixty-five patients treated, the results were complete recovery in more than 15 per cent and amelioration in 75 per cent.

ANDERSON, Philadelphia.

NERVOUS CONTROL OF XANTHOPHORE CHANGES IN FUNDULUS. E. F. B. FRIES. Nat. Acad. f. Sc. **13**:567 (Aug.) 1927.

The possibility of a pigment-motor center in the brain is discussed. There is evidence that these fishes have some such mechanism, but it does not account for all the phenomena described; there is a certain amount of color adaptation to the environment even in the areas of denervated skin. The author ascertained the innervation of the xanthophores of *Fundulus* by fibers which carry impulses from the medulla, as in the case of the melanophores.

COBB, Boston.

EFFECT OF FORMALIN ON THE VELOCITY OF THE WASSERMANN REACTION. C. E. REYNER, Am. J. Syph. **2**:233 (April) 1927.

The author added a minute quantity of liquor formaldehydi to diluted antigen and observed the effect on the speed and intensity of the Wassermann reaction. Serums of twenty-five syphilitic and of twenty-five nonsyphilitic patients were tested by the Kolmer and the Kolmer-formaldehyde methods. It was found that the addition of formaldehyde greatly increased the speed of the reaction and also produced a greater degree of fixation. Technic and charts are given in detail, and the practical advantages of this modification are discussed.

KUBITSCHEK, Philadelphia.

Society Transactions

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Regular Meeting, Oct. 20, 1927

HENRY R. VIETS, M.D., *President, in the Chair*

DR. DONALD GREGG gave an interesting account of the recent meeting in London.

EPILEPSY AND PARKINSONISM. DR. PAUL I. YAKOVLEV.

In the symptom complex of epidemic encephalitis and its residuals, convulsions are not uncommon. A. Wimmer qualifies these convulsions as "epilepsy in chronic epidemic encephalitis." They belong to the symptomology of the active, chronic, toxi-infectious process in the central nervous system, rather than to the symptomatology of truly postencephalitis residuals or sequelae sensu strictu.

The parkinsonian syndrome is the most common of these postencephalitic sequelae. In the course of examination of several hundred epileptic patients in Monson State Hospital, a special group of patients with a more or less late onset of epilepsy, following epidemic encephalitis, was observed. Two patients with such encephalitic epilepsy later developed the neurologic picture of parkinsonism and showed an interesting relationship between the development of this syndrome and the frequency of convulsions.

CASE 1.—S. M., a man, aged 31, had epidemic encephalitis in 1918. Four years later, he began to have epileptiform convulsions on an average of one a week. In 1926, the attacks became milder and not so frequent—one or two each month—but he began to feel stiffness in the muscles. When he was examined at that time, mild signs of latent parkinsonism were discovered and were more marked on the right side; slight cog-wheel tremor of the tongue and fingers, and lack of facial expression. During the next seven months he had only two or three attacks, but muscular rigidity, tremor, cog-wheel movement, lack of associated movements and other signs of parkinsonism increased notably in intensity.

CASE 2.—E. C., a colored man, aged 24, with an unimportant family history, had been in good health up to the age of 13 or 14 when he had had one convulsion, which was attributed to indigestion. About one year later, in 1918, at the age of 14, he had epidemic encephalitis. Since that time he had shown characteristic changes in personality with some mental enfeeblement. About two years later he began to have convulsions which gradually grew more severe and more frequent up to 1921, when he first noticed the subjective signs of rigidity. In 1922, he was admitted to Monson State Hospital and showed marked slowness of movements and motor inertia. The spells became only occasional and since 1923, up to the present time, he has had none, while the rigidity has reached an extreme degree. The clinical picture at the present time represents a typical example of postencephalitic parkinsonian syndrome; it has remained unchanged for the last four years.

Among my own cases of parkinsonian rigidity, I have not observed convulsions as part of the syndrome; among the observations of many reliable authors I have not been able to find an example of such an occurrence.

The problem of the relationship between the evolution of epileptic paroxysms and the evolution of extrapyramidal rigidity is not confined to encephaltic epilepsy and postencephalitic parkinsonism, but seems to be based on a larger

clinical ground. In the course of epileptic deterioration, whatever its etiology, in addition to the characteristic mental changes, even more characteristic neurosomatic changes are observed. Among these neurosomatic symptoms in epileptic patients, the extrapyramidal signs of the group of parkinsonism, at first faint and later more definite, are especially common. Of 300 more or less deteriorated patients at the Monson State Hospital, one-half showed this extrapyramidal symptom either in pure form or associated with other organic extrapyramidal, pyramidal and sometimes cerebellar signs. The clinical history in one such case may serve as an illustration.

Case 3.—L. C., a man, aged 49, with a family history of no significance, had shown an apparently normal development, except that he always seemed to be somewhat duller than his brothers and sisters. There was no history of venereal disease. The man married at the age of about 24; children were born and there were no miscarriages. At the age of 30, he began to have convulsions which appeared almost every day and which were severe. With the onset of convulsions, he gradually developed mental enfeeblement. Active and laborious, a shoemaker by trade, he became unable to sustain himself, and after being under the partial charge of members of the family for several years, he was placed in Monson State Hospital, mostly on account of his mental deterioration. The spells became much rarer, and for the past four or five years he has developed gradually a neurologic picture resembling that of paralysis agitans: characteristic attitude of body, muscular rigidity, tremor, lack of associated movements and motor inertia. The Wassermann reactions with the blood and spinal fluid have been repeatedly negative. The attacks continue to diminish in frequency, and for the past year he has had an average of three attacks a month instead of almost daily as he had about five years before.

In 1926, Urechia and Elekes described the case of a chronic epileptic man, aged 42, who about three years before death developed gradually a typical parkinsonian syndrome, while the convulsions which he had had all his life disappeared. Postmortem microscopic examination showed marked degenerative changes in the region of the basal ganglia without evidence of an inflammatory process.

In 1926, Toulouse, Marchand, Bauer and Male presented at the meeting of the Paris Clinical Society of Mental Medicine two adult epileptic patients, with the onset of epilepsy in earlier childhood and subsequent gradual mental deterioration. Both patients showed a typical picture of a parkinsonian syndrome.

In speaking of neurosomatic deterioration in epilepsy, I prefer the somewhat vague term "parkinsonism" to the more specific term parkinsonian syndrome. Indeed, if sometimes there is an analogy between the picture of the deteriorated epileptic patient and the parkinsonian syndrome, such as develops in cerebral arteriosclerosis, cerebral syphilis, and especially after epidemic encephalitis, this is mere analogy and not necessarily identity. In epileptic deterioration, mental changes constitute too important a component to be overlooked, while in the parkinsonian syndrome proper, the mental changes recede far into the background if they are present. The signs of parkinsonism in epileptic deterioration develop and persist in pure form only in a minority of cases. In the majority of epileptic patients, symptoms of parkinsonism are usually associated with signs of other semiologic type, especially with symptoms of corticopyramidal involvement. The last association of extrapyramidal and pyramidal symptoms in conjunction with mental enfeeblement often results in a picture that closely resembles pseudobulbar palsy. Paradoxically enough, the symptom complex of pseudobulbar palsy in epileptic patients is observed almost exclusively at the two extremes of life. In the aged, senile pseudobulbar palsy occurs, and in children, aged from 8 to 15, juvenile pseudobulbar palsy.

The following case illustrates the last clinical variety:

CASE 4.—G. M., a boy, aged 15, with an unimportant family history, had a normal birth and development up to the age of 4 or 5. Then, without obvious cause, he began to have convulsions on an average of from fifteen to twenty each month. At the same time, he showed marked delay in mental development. At the age of 12, he was admitted to the hospital, when he was found to have a mental age of 5 years, though physically he was about normal. During the first year in the hospital, he had an average of fifteen attacks a month. In 1926, he began to show impairment, not only mental but also physical. He became more fond of bed and did not want to play with other children. Neurologic examination at the end of 1926 showed: Marked mental enfeeblement—the boy was almost idiotic—face immobile, lower jaw drooping, saliva drooling over the lower lip, swallowing and mastication difficult so that he had to be fed, and choked frequently; he did not speak spontaneously, but when he could be induced to do so, he answered questions in a monotonous monosyllabic manner, pronouncing the words at the end of expiration and with considerable dysarthria. He stood and walked chiefly on the toes, with the extremities in flexion, the trunk brought forward and the head bent on the chest. There was marked tremor of both arms, hands and fingers, and sometimes of the feet. On passive movement, marked rigidity was found; the action of the antagonists were exaggerated; cogwheel rhythm was distinct. When he walked, there was marked lack of associated movements; in movements of the lower limbs there was a pyramidal spasticity and hypertonic rigidity. The tendon reflexes were exaggerated and hypertonic, that is, associated with exaggerated reaction of the antagonists; they were more ample on the left side. The plantar reflexes were: constant extension on the left; usually extension, sometimes flexion, on the right. Clonus was present on both sides. The abdominal reflexes were present. The blood Wassermann reaction was negative. Since the onset of the rigidity, the number of attacks during 1926 decreased from an average of fifteen to an average of ten a month.

During the past eight months, the rigidity has markedly progressed. When in bed there is a more pronounced tendency to keep the lower limbs tightly flexed on the body in the attitude characteristic of cerebral flexion paraplegia. The number of attacks continues to decrease; according to records for 1927, they average only five a month.

The reduction or even disappearance of convulsions with advancement of extrapyramidal muscular rigidity noted in the cases cited is frequent. Three hundred cases of epilepsy were studied from the point of view of organic nervous semiology. When grouped according to age and relative duration of the epilepsy, it appears that the older the patient and the longer the duration of the epilepsy the more frequent are symptoms of extrapyramidal rigidity, while a frequency of epileptic attacks decreases. About one third of twenty-four patients in the first ten years of life, with an average duration of epilepsy of five years, had shown signs of muscular rigidity; the average number of grand mal attacks in this group was nine. Of ninety-seven patients in the second decade of life, with an average duration of epilepsy of ten years, about 40 per cent had shown more or less advanced muscular rigidity; the average number of spells in this group was six grand mal attacks a month. Of eighty patients in the third decade, with an average duration of epilepsy of sixteen years, 48 per cent had shown muscular rigidity; the average number of spells in this group was four grand mal attacks a month. Of forty-six patients in the fourth decade of life, with the duration of epilepsy of twenty-three years, 67 per cent had shown muscular rigidity; the average number of attacks in this group was four grand mal attacks a month. Of twenty-eight patients in the fifth decade, with an average duration of epilepsy of twenty-six years, 50 per cent had shown muscular rigidity; the average number of spells in this group was three grand mal attacks a month. Of twenty-five patients

aged from 51 to 70, with an average duration of epilepsy of twenty-two years, 72 per cent had shown muscular rigidity; the average number of spells in this group was two or less grand mal attacks a month.

Such are the clinical facts. Are they coincidental or interrelated? This is a subject for further observation. I think that in the evolution of epileptic deterioration the clinical symptoms of extrapyramidal rigidity (parkinsonism) are extremely characteristic; with advancement of the rigidity, that is, with the gradual wearing out of the subcortical functional level, the convulsive reaction capacity of the central nervous system diminishes.

DISCUSSION

DR. PERCIVAL BAILEY: What did lumbar puncture show in case 4?

DR. YAKOVLEV: It gave negative results. The albumin was not increased. The Wassermann reaction was negative in both blood and spinal fluid.

AUDITORY HALLUCINATIONS PROVOKED BY INTRACRANIAL TUMORS. DR. CYRIL B COURVILLE.

Hallucinations of smell, taste and vision are of frequent occurrence in cases of tumor of the brain, but little if any attention has been paid heretofore to auditory hallucinations. In the surgical clinic of the Peter Bent Brigham Hospital, although as a routine patients are asked about visual, olfactory and gustatory phenomena and a negative answer is always included in the history, a similar question is not asked about auditory hallucinations. The probable reason for this is that cortical auditory phenomena are not well known. There are tests by which one can easily distinguish the minutest lesion of the visual cortex, but such tests do not exist for the investigation of the auditory cortex. Dr. Harvey Cushing has remarked that in cases of tumor of the brain auditory disturbances are conspicuous by their absence. Attempts made in this clinic by Dr. Theodore Green to develop methods of testing cortical auditory function did not meet with much success. It seemed nevertheless of interest to determine whether records of auditory hallucinations occur in the clinical histories of the hospital. Whatever has been discovered has been information volunteered by the patients or by their relatives and had not been elicited by direct questioning.

I have examined the records of 412 verified cases of tumor of the brain. Of these, 98 were tumors in the frontal lobe, 171 in the parietal lobe, 44 in the occipital lobe and 99 in the temporal lobe. Tumors of the parietal and occipital lobes can be dismissed without further notice because nothing resembling auditory hallucinations was found in association with them. The cases showing auditory hallucinations may be divided into three groups: (1) tumors of the frontal lobe, (2) tumors of the temporal lobe and (3) multiple tumors of the brain.

In group 1 are six cases in which the patients had definite auditory hallucinations. In all but one, the hallucinations were those of voices. In these cases there was also evidence of great increase of intracranial pressure with definite mental changes amounting to a psychosis. In group 2 were four cases in which there were definite auditory phenomena. With the exception of one case, the mental changes characteristic of those in the frontal lobe were inconspicuous; here and there was only slightly increase intracranial pressure. One case of suspected tumor of the temporal lobe has been included in which auditory hallucinations developed after subtemporal decompression and probing of the lobe in an attempt to locate the tumor; the phenomena probably resulted from trauma to the area involved. Group 3 is composed of two cases of multiple metastatic tumors of the brain. The first patient, a man, aged 55, had tumors in the right temporal lobe, in the right and left parietal, and in the left occipital lobes, with definite auditory hallucinations, temporary attacks of mental aberration, and early choking of the optic disks.

The second patient, a woman, aged 53, had multiple tumors, three of them in the right frontal lobe, another in the left frontal, and others in both temporal lobes, the basal ganglia and the peduncles of the cerebrum and the cerebellum. In these instances, the frontal and temporal lobes were involved as well as other areas; in the light of the previous observations, the auditory phenomena probably resulted from involvement of these lobes.

It is perhaps a matter more of interest than of importance that the tumors in twelve of the thirteen cases cited were in the right hemisphere, although in several cases both hemispheres were involved. In one instance the lesion was apparently confined to the left temporal lobe, this being the only case of the series not coming to autopsy.

Phenomena, therefore, which are considered as possible auditory hallucinations were observed in cases of solitary tumor only when located in the frontal and temporal lobes. Moreover those in the frontal lobe were associated with other hallucinations, optic, olfactory and gustatory, with marked mental disturbances other than hallucinations, and with pronounced pressure symptoms; on the other hand, those observed with tumors of the temporal lobe were not associated with mental symptoms other than visual hallucinations of known temporal lobe origin. It would seem, therefore, that those auditory hallucinations associated with tumors of the temporal lobe might be considered as of the nature of focal symptoms while those with lesions of the frontal lobe might be due to distance phenomena of increased intracranial tension, or they might be part of the psychosis incident to the organic lesion, or both.

Details of the observations are given in the accompanying table. In describing the auditory symptoms the exact words of the record are transcribed.

DISCUSSION

DR. PERCIVAL BAILEY: I have been interested for some time in the fact that we did not ask the patient about auditory hallucinations in taking a history. When I returned to the Peter Bent Brigham Hospital in 1926, I intended to search the records for instances of auditory hallucinations, and told Dr. Tracy Putnam that I had never found a tumor of the brain associated with auditory hallucinations. Dr. Putnam knew of one such case, and when Dr. Courville came to the hospital, we set him the task of finding records of patients who had auditory hallucinations. Most of the information was volunteered by the patients or their relatives. What was found in the histories is suggestive, not demonstrative, but enough to suggest a search in all cases of tumor of the brain for auditory hallucinations. Dr. Vincent of Paris has told me of a case of tumor of the brain in the temporal lobe in which definite auditory hallucinations were present, and I have no doubt they could be found more often, if systematically sought.

DR. TRACY PUTNAM: Dr. Courville has had a tedious task collecting these facts, but the result is worth while. One is, perhaps, not justified in supposing that the hallucinations of hearing due to tumors in the temporal lobe are necessarily due to irritation of the auditory cortex. Judging from the analogy of visual hallucinations, it is perhaps even unlikely that the auditory cortex itself is involved. Henschen's original view that visual hallucinations were due to irritation of the striate area has been disproved and, in tumors at least, hallucinations are much more common with lesions of the temporal lobe than with those of the occipital lobe. Moreover, the fact that in so many cases visual and auditory hallucinations coexist is perhaps an indication that they are both due to stimulation of some higher cortex. I think all will find a much larger proportion of auditory hallucinations in the future.

DR. COURVILLE: I am glad that Dr. Putnam brought out this point. I have examined the records of all verified cases of tumors of the brain, and it was interesting to observe optic hallucinations of a more or less definite nature in tumors of every lobe of the brain. In other words, optic hallucinations were the most general of all the phenomena of this nature. Olfactory

Surgical Number	Auditory Hallucinations	Other Hallucinations			Pathologic Condition	Pressure Symptoms	Mental Symptoms
		Olfactory	Visual	Gustatory			
		Group 1.—Tumors of the Frontal Lobe					
4663	During the day will often be in a dreamy state, but is able to recognize husband and says that she knows but is unable to carry on any rational conversation for she lapses into these dreamy states "Following a dream, carried on for three days, namely April 19, 20 and 21, conversation with an imaginary person according to her husband"	"For the past 1½ years she has experienced an odor in her nose like decayed flesh"	Suggested under auditory	0	A tumor located in the inferior portion of the right frontal lobe, extending back to the tip of the temporal lobe on the right side; microscopic examination showed it to be a glioma	Severe headaches, projectile vomiting, high choked disks, 5 diopters elevation on both sides	Disorientation, loss of memory, irritable, dreamy mental states
14311	"Patient imagined that a still was being run in a house across the street, as she complained of the noise made by the still"	0	0	0	A tumor lying close to the falx and in the upper portion of the right frontal lobe; microscopic examination showed it to be a glioma	Headaches, nausea and vomiting, choked disks, 3 diopters bilaterally	Periods of complete disorientation and frequent delusions, mental confusion, stupor at times
15863	"Frequently she imagines that her daughters and sons are with her, speaking to them in a quiet, advisory tone" Subsequent history from Yale University Hospital reports, "Frequent hallucinations of sight and hearing"	0	Saw imaginary faces of human beings or animals	0	Endothelioma weighing 140 Gm., straddling the falx and adherent to the frontal fossa, extending back to the sella turcica	Headaches, projectile vomiting, atrophy of both optic disks, blood pressure 200/78	Disorientation, delusions
19244 19081	"For the past two weeks the patient fairly frequently thought that he heard his children when he did not; further auditory hallucinations could not be brought out by questioning the wife"	0	Thought he saw people pass his door when none were present	0	A massive posterior right frontal cystic glioma, containing 50 cc. of fluid	Frontal headaches, projectile vomiting, 3 diopters elevation of the disks	Loss of memory, querulous, critical, careless in dress
20125 23917 25020	"There have been occasional visual hallucinations as seeing her children and talking to them when they were away. Auditory hallucinations of a similar nature have been noted"	0	Suggested under auditory	0	A large tumor of the lower part of the right frontal lobe extending over into the left frontal and back to, but not involving, the right parietal lobe, oligodendroglioma	Fontal headaches, vomiting, choked disks, 5 diopters right, 4 diopters left	Quarrelsome, obstinate, loss of memory, euphoric

22359 26637 28293 28338	"For the past four or five weeks the patient has suffered from a roaring in the head like the blowing of wind through the trees. This has not been confined to the ears but has been sensed all over the head" "For the past two nights the patient has had auditory hallucinations. He though his sister was calling for help outside his door and that at least three people were killed outside his door by cracking their heads"	"He thought there was gas escaping in the room"	0	0	Necropsy demonstrated a massive bilateral tumor of the frontal lobe arising from the frontal fossa and straddling the falx; endothelioma	Headaches, 3 diopters elevation of right disk, primary optic atrophy on left	Marked changes in personality and habits, forgetful, indolent, unmindful of business affairs, catatonic states
			Group 2.—Tumors of the Temporal Lobe				
43	"Although there has been no definite tinnitus complained of, the patient at the onset would often ask members of the family at the table what they were saying when in reality everything had been quiet"	0	0	0	Large degenerated glioma of the left temporal lobe involving the entire anterior portion; it was beneath the posterior portion of the frontal lobe; microscopic examination revealed spongioblastoma multiforme	Severe headache, blood pressure 200 systolic, marked choking of the disks (elevation not stated), convolutional atrophy shown in roentgenogram	Marked mental changes, disorientation, loss of memory, mental confusion
582 968 10322 10555	(Right, subtemporal decompression done March 6, 1914) "On April 17 (1914) patient developed a severe headache in the right temporal region. Decompression area became tense and painful to pressure. During the evening patient began to have hallucinations of hearing. She thought people were knocking at the door and heard telephone conversations"	0	"Saw colored lights on the walls, processions of queer figures marching along the ceiling"	0	Old gliomatous cyst of the left temporal lobe with cavity about the size of a pigeon's egg	Spells of acute headache, nausea and vomiting, tight decompression area, early choking of the disks; no elevation	No definite mental changes
18801	"Five months ago she awakened her husband because she thought she heard an automobile outside. These hallucinations persisted for several weeks and then disappeared"	0	"Saw circles of light off to either side like a new moon"	0	Grayish-brown soft tumor in the posterior end of the right superior temporal gyrus; glioma	Headaches, vomiting, choked disks, from 3 to 4 diopters elevation	No definite mental changes

Auditory Hallucinations and Other Symptoms in Patients with Tumors of the Brain—Continued

Surgical Number	Auditory Hallucinations	Other Hallucinations			Pathologic Condition	Pressure Symptoms	Mental Symptoms
		Olfactory	Visual	Gustatory			
22383 25231 28546	"On several occasions while working in the shop he felt that he heard people singing far away. It sounded funny to him. He could not recognize the tune or the people. This occurred two or three times. It will be noted that before his operation he also had hallucinations of hearing which he describes as wind blowing through the trees or whistling which he remembers now, having had similar phenomena before"	0	"On one occasion a few weeks ago had a strange spell in which he saw large wild animals in front of him. They gradually faded away"	0	Huge protoplasmic glioma of the right temporal lobe about the size of a goose egg	Headaches, projectile vomiting, early choking of the disks, no measurable elevation	Minor personality changes, irritability, forgetfulness, dreamy states
18273	(Right temporal lobe tumor suspected; right subtemporal decompression and exploration) "Has had two strange attacks since operation, one yesterday and one this morning about 3 a. m. During two or three minutes he heard music as of a grindorgan or phonograph off to his left. The pain in his head disappeared during the attack. He seemed to feel as though he were in a different world"	0	0	0	A right temporal lobe suspect; decompression done and no tumor found after repeated probings of the temporal lobe	No headaches, no projectile vomiting, no choking of the disks, bilateral secondary atrophy	No mental changes
		Group 3.—Multiple Tumors (Metastatic)					
15440	"Complained of hearing bells and bands"	0	"Saw ships of various denominations and other objects which were passing along the wall. Calls out to imaginary people"	0	Multiple metastatic tumors of the brain from a primary carcinoma of the lung; one found in the right temporal lobe, one in the right parietal lobe, one in the left parietal lobe, and one in the left occipital lobe	Headaches, projectile vomiting, blood pressure 160/80, early choking of the optic disks, no measurable elevation	Temporary spells of disorientation, confusion, and delirium, with delusions
22539	"Her son states that she complained of hearing noises such as a running victrola, violin, etc., when there was none about"	Smelled tobacco smoke when there was none about	Saw objects moving about especially on the right side	0	Multiple metastatic tumors of the brain from a primary carcinoma of the breast. Three tumors were found in the right frontal lobe, one in the left fontal lobe, multiple small nodules in both temporal lobes, also in the basal ganglia, and in the cerebral and cerebellar peduncles	Severe frontal headaches, choking of the disks, 3 diopters bilateral	Marked disorientation, drowsiness, apathy, and lack of mental concentration

hallucinations were occasionally found in patients with tumors of the frontal lobe, although I attribute this phenomenon to lesions of the temporal lobe. Auditory hallucinations were found only in cases of tumors of the frontal and temporal lobes as I have indicated. The hallucinations in the cases of tumors of the frontal lobe were usually described by the relatives of the patient, while those in patients with tumors of the temporal lobe were volunteered, as a rule, by the patient himself. One patient with a tumor of the tip of the left temporal lobe, underlying the frontal lobe and possibly involving it, had a definite psychosis. It must be remembered that in all cases of tumor of the brain with increased intracranial tension, symptoms may arise from pressure at a distance from the actual primary lesion.

DR. E. W. TAYLOR: It is a matter of some interest that the tumors which produced such hallucinations were largely on the right side. I will ask Dr. Courville whether that, in his opinion, was merely a coincidence, or whether there was a definite reason for it.

DR. COURVILLE: I attach no significance to it. Probably in the next thirteen patients with auditory hallucinations the tumors will be on the left side. It was a matter of interest that eleven of the twelve proved tumors were on the right side. Some time, when one knows more about the auditory mechanism, one may find some importance in this observation, but at present no definite conclusions can be drawn.

DR. H. R. VIETS: When Dr. Horrax spoke about visual hallucinations a few years ago, he pointed out that patients with hemianopia often had hallucinations of sight on the blind side. Did any of these patients have deafness, and could they localize, either right or left, from whence the hallucinations appeared to come? Dr. Courville said nothing about acoustic neuroma tumors. Do patients with tumors of the eighth nerve have hallucinations or merely tinnitus?

DR. COURVILLE: I have not looked up the cases of acoustic neurinomas. At the clinic we were interested in the question of cortical involvement, and deafness was not present in any case, as I remember. Several patients said that the auditory hallucinations were preceded by a distinct ringing in the ears which could would be classified as tinnitus. At a later time, these patients developed definite auditory hallucinations. In only one case did the symptom seem to be lateralized, and that in a tumor suspect with a decompression; the right temporal lobe was examined, and the patient seemed to have auditory hallucinations to his left. This is the only case in which the record gives any information as to lateralization.

DR. BAILEY: I have never come across an observation of that kind, but have not searched the records for it. In one case of tumor of the pineal body there was definite tinnitus, deafness in one ear and then in the other. I do not remember having noted definite auditory hallucinations associated with acoustic neurinomas.

DR. E. S. ABBOTT: Because hallucinations occur in cases of tumor of the brain, it does not necessarily follow that the tumor is the cause of the hallucinations. I have been wondering whether in these cases, the matter of drugs that the patients might have been taking had been considered. Some patients are susceptible to hallucinations after rather small quantities of ordinary opiates and sedatives. I have seen a patient with definite visual hallucinations after having taken about 0.5 grain (0.032 Gm.) of codeine. Another patient had auditory and visual hallucinations after an ordinary dose of barbital. This patient was given two ordinary doses during an evening and had active hallucinations which on one occasion lasted for two days. Pain, headache and insomnia not infrequently occur in cases of tumor of the brain. Opiates or sedatives may have been prescribed, or taken without prescription, in the case of some of the patients whose cases have been reported, either before or after admission to the hospital. If the existence of a causal relationship is

to be determined between hallucinations and tumor of the brain, it is necessary to eliminate all other possible or probable causes of hallucinations in these particular cases—and there are many in addition to drugs.

DR. E. B. LANE: I listed hallucinations in several hundred patients years ago. A large proportion of the hallucinations were auditory, and by far the majority of auditory hallucinations were spoken words. In this list, Dr. Courville has noises about equal to those of the spoken word. In several hundred cases the ringing of bells, shouting and other sounds were in the minority, comprising about 10 per cent, I should say, of all auditory hallucinations.

DR. COURVILLE: I was much interested in the last remark. Most of the hallucinations of hearing in these cases seemed to be of the spoken voice or of music. The voices were rather characteristic of the tumors of the frontal lobe. Those of the temporal lobe were varied in nature. One cannot draw conclusions from these cases concerning the type of hallucinations.

DR. VIETS: Did drugs play a rôle in any of these cases?

DR. COURVILLE: Dr. Cushing does not give sedatives in cases of tumor of the brain. At any rate, they were probably not a factor in the patients with tumors of the temporal lobe who had few if any striking subjective discomforts. But it is impossible to say definitely whether any of these patients had taken drugs, as many of them were outside the hospital at the time the hallucination occurred.

DR. BAILEY: These are old records. The medicine a patient has been given before he comes to the hospital is seldom noted. This paper is not presented as a scientific contribution, but as an interesting indication of what may be found if one searches for these phenomena carefully in cases of tumor of the brain.

PHILADELPHIA NEUROLOGICAL SOCIETY

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M. A. BURNS, M.D., *President, in the Chair*

CORRELATION OF CLINICAL AND PATHOLOGIC DIAGNOSES IN HEMIPLEGIA. DR. F. N. ANDERSON.

This paper presents the results of an analysis of 173 cases of hemiplegia, in which an autopsy was performed at the Philadelphia General Hospital in 1924, 1925 and 1926. A few cases of hemiplegia are included which were not diagnosed clinically as hemiplegia, and a few cases of clinical hemiplegia in which other pathologic conditions were present. The immediate concern was to ascertain the relative accuracy of differentiation between thrombosis and hemorrhage. Since many clinicians teach that it is possible to separate these two, diagnoses should not indicate merely hemiplegia or "stroke," but an attempt should be made to determine which of these conditions is present. Several other observations developed during the study.

The clinical diagnoses were divided as follows: thrombosis, 69 cases (40 per cent); hemorrhage, 44 cases (25.4 per cent); not stated, 43 cases (24.9 per cent), and total additional, 17 cases (9.8 per cent). The last heading includes a multiplicity of diagnoses, such as posterolateral sclerosis, syphilis and other conditions; the number represents a normal error in diagnosis. It is significant that in one fourth of the cases in this series an attempt was not made to differentiate between hemorrhage and thrombosis. Furthermore, one fourth of all cases were diagnosed hemorrhage. Undoubtedly if each clinician was asked the ratio of hemorrhages to thromboses he would answer not more

than 1:10. (Naturally other factors are at work here, such as a tendency for patients with thrombosis to improve and go home.)

The pathologic diagnoses in these 173 cases were: thrombosis, 116 cases (67 per cent); hemorrhage, 22 cases (12.7 per cent); both hemorrhage and thrombosis, 9 cases (5.2 per cent); arteriosclerosis, 8 cases (4.7 per cent), and total additional, 18 cases (10 per cent). It will be noted that two thirds of all cases of hemiplegia studied at autopsy at the Philadelphia General Hospital are due to thrombosis. Almost one half as many cases are listed pathologically as showing both hemorrhage and thrombosis as those showing hemorrhage alone. The addition of this group to the thrombosis group would make relatively little difference; whereas, addition to the hemorrhage group would materially alter the percentage conclusions drawn. Usually there was a thrombosis in one part of the brain and a hemorrhage in another. A correlation of the clinical and pathologic diagnoses is shown in the table.

These checkings account for 84.3 per cent of the cases; the remaining 15.7 per cent (27 cases) represent almost as many different combinations: uremia-abscess, thrombosis-tumor and other conditions. This means that 36 per cent of all hemiplegias were correctly diagnosed. The side involved was: right, 78 cases (45.1 per cent); left, 69 cases (40 per cent); both sides, 14 cases (8 per cent); undetermined, 11 cases (7 per cent). At first glance it may

Correlation of Clinical and Pathologic Diagnoses

Clinical Diagnoses	Pathologic Diagnoses	No. of Cases	Percentage
Thrombosis	Thrombosis	49	28.3
Hemorrhage	Hemorrhage	13	7.5
Thrombosis	Hemorrhage	13	7.5
Hemorrhage	Thrombosis	27	15.6
No diagnosis	Thrombosis	43	24.8
No diagnosis	Hemorrhage	1	0.6

appear that the number in which the side of the lesion was undetermined is large, but not all of these were diagnosed as hemiplegia. Four were listed as uremia. In two or three instances, however, it was impossible to determine on which side the hemiplegia existed. Thirty patients (about 17 per cent) suffered more than one stroke. Of these, twenty-six had two strokes, two had three, one had four, and one had six. Fourteen of the multiple strokes were repeated on the right, eight were repeated on the left, and eight were repeated on the side opposite from the original. Judging from this one might tentatively say that chances favor a recurrent stroke on the side originally involved.

The location is extremely difficult to present with certainty, because almost every possible combination occurred. Using only a few main headings, the locations were: basal ganglia region, 37 cases (21.3 per cent); cortex, 57 cases (33 per cent); multiple, 53 cases (30.6 per cent); cerebellum, 4 cases (2.3 per cent); corpus callosum, 3 cases (1.7 per cent); thalamus, 6 cases (3.5 per cent).

Loss of consciousness was present in 50 cases (29 per cent); was absent in 48 cases (27.7 per cent), and not determined in 74 cases (42.8 per cent). Loss of consciousness was present in 27 of 116 cases (23.3 per cent) of thrombosis; in 19 of 22 cases (86.4 per cent) of pure hemorrhage, and in 23 of 31 cases (74.2 per cent) of combined hemorrhage and thrombosis.

The occurrence of unconsciousness was probably one of the most interesting observations from the study. There was a large group of cases in which no record of this symptom was made; only those in which a definite statement of the condition of consciousness was reported have been included. It may be that loss of consciousness is more frequent in hemorrhage, but it is evident that

unconsciousness occurs in three fourths of all cases of hemorrhage, and in less than one fourth of cases of thrombosis.

The Wassermann reaction was positive in 12 cases (6.9 per cent); negative in 86 cases (50 per cent), and not determined in 75 cases (43.4 per cent).

The average length of residence in hospital was just above six months, with a maximum of twelve years and three months in one case.

The average age was for males, 62 minus; for females, 64 minus, and for the group, 62 plus.

Aphasia was present in 79 cases (45.7 per cent); absent in 15 cases (8 per cent), and unknown in 79 cases (45.7 per cent).

The blood pressure averaged systolic in 74 cases, 155 mm., and diastolic in 74 cases, 92 mm. In 48 cases of thrombosis the averages were: systolic 154, and diastolic 74. In 18 cases of hemorrhage the averages were: systolic 183, and diastolic 105.

DISCUSSION

Dr. Walter Freeman: The differential diagnosis between cerebral hemorrhage and thrombosis is not always satisfactory, even at necropsy. In certain instances of thrombosis, hemorrhagic infarction results, peppering the cortex with petechial hemorrhage, which in later or severer stages may reach hemorrhagic infiltration. In the fresh state this will resemble hemorrhage. In the course of time the blood is absorbed and the necrotic cerebral tissue undergoes liquefaction and absorption, so that in the late stages typical symptoms of thrombosis are observed. Dr. Anderson mentioned the association of thrombosis and hemorrhage in certain cases, and here I imagine the basic lesion was thrombosis. In the living patient one cannot always distinguish between thrombosis and hemorrhage, even if one observes the condition from its inception. Certain cases of extensive thrombosis, particularly when it involves the internal carotid, will give rise to deep coma and even death within a few hours. On the other hand, patients with small hemorrhages have lived for weeks and died of some other illness. The clinical diagnosis of cerebral thrombosis is made and hemorrhage is found at necropsy. According to LeCount, nitrogen retention furnishes an accurate diagnostic feature in differentiating cerebral accident from uremia, since the urea nitrogen is about four times as high in the latter as in the former. In the differential diagnosis between cerebral hemorrhage and cerebral thrombosis, a bloody spinal fluid will immediately point to hemorrhage, but certain hemorrhages are concealed and do not break through either into the ventricles or externally. Hemorrhage into the cerebral substance is not necessarily fatal. In a series of patients that I studied, five lived more than a week, two more than five weeks, and one died with a second hemorrhage on the opposite side four months after the first attack.

Dr. Anedrson: The cases reported were characteristic for all cases of hemiplegia as admitted to the hospital. A few cases of uremia were clinically diagnosed; two were thrombosis and one was an abscess. The question was raised as to tumor and two cases were hemorrhages into a tumor.

A Case of Tabes Dorsalis with Thrombosis of the Spinal Arteries. Dr. Norman Peterson. (From the service of Dr. T. H. Weisenburg in the Infirmary for Nervous Diseases.)

A chemist, aged 45, in 1904 or 1905, contracted syphilis and for the following three years took biniodide of mercury by mouth. In 1922, he was suddenly seized with a sharp shooting pain in the abdomen and with vomiting. The attack lasted two or three days, but for two weeks after this he had a sick feeling in the epigastrium. From that time until 1925, he would have such an attack once a month or more. Roentgen-ray studies in 1922 and 1923 showed gastroptosis. Of various treatments administered, an abdominal binder relieved the pain more than any other.

In 1923, he went to the Jefferson Hospital where the condition was diagnosed as tabes dorsalis, and antisyphilitic treatment was instituted. He was given twenty-six intravenous injections; numerous lumbar punctures were made, and potassium iodide was administered by mouth. About the time when the abdominal pain began to clear up, in the beginning of 1925, he noticed numbness which extended down the inner aspect of each arm and included the fourth and fifth fingers. One month later he suddenly became unable to use his hands properly when he was changing an automobile tire. He changed the tire correctly, but was unable to screw the cap on the valve. The hands seemed numb, and, although he knew that he held something in his fingers, he could not tell in what position he held it; he could not grasp it tightly and retain it in his hand. Notwithstanding this he drove the car home. The next day he could not drive the car as he was unable to lift the arms at the shoulders. The disability seemed to be chiefly in the back of the neck and in the shoulders. Three or four days later he began to have lightning pains in the back of the neck, the shoulders and the arms. These have persisted since but are not as frequent as before. When the pain occurs, the part involved stiffens, so that he throws the head back or forward in an effort to overcome the pain. Ten days after the onset the hands became clumsy, and movements became awkward and incoordinate. This clumsiness is much worse in the dark. Last winter he had incontinence, but for two or three years previous to that could go a considerable time without voiding. Last winter also he had frequent painful desire to defecate but could not do so at the time. He has no symptoms referable to the legs except that he cannot go up a flight of stairs in the dark; he does not measure the distance between steps properly and tends to fall forward. He has no bulbar symptoms.

Examination.—The left pupil was larger than the right and was acircular. Neither pupil reacted to light although both reacted in accommodation; otherwise there were no involvements of the cranial nerves. There was atrophy of the muscles of both shoulder girdles, more marked on the right side. The muscles chiefly involved were the deltoids, supraspinati, infraspinati and the upper part of each pectoralis major. The muscles of the upper arm were involved to a lesser extent. The right shoulde girdle dropped; movements of it were much restricted. On the left side there was diminution but it is not as marked. Fibrillary twitchings and myoedema were observed in the atrophic muscles. There was no atrophy or weakness of the lower extremities. All movements of the upper extremities were incoordinate and sense of position was lost in these members. In the lower extremities there was no incoordination and no loss of sense of position in the heel-to-knee test or in movements of individual joints. Appreciation of all sensation was delayed over the body. There was impairment of pain sensibility over the chest from the level of the fifth to the seventh dorsal segment. There was hyperalgesia over the right infraclavicular fossa, right deltoid muscle, left infraclavicular fossa, left shoulder girdle and left arm. Tactile sensibility was impaired from the nipples to the costal margins, on the inside of the arms and over the hands. Touch over the hands was appreciated as pain and was not localized. Vibratory sense was lost over the sacrum and was impaired over the patellas, anterior superior spines and both arms. Slight differences in temperature were not discriminated though extreme variations were, if a sufficient interval was left between the application of the stimuli and if the stimulus was applied for a sufficient length of time. The abdominal and cremasteric reflexes were present; all tendon reflexes were absent and the plantar response was flexion on both sides. The gait was slightly ataxic and there was a positive Romberg sign.

In December, 1925, the blood Wassermann reaction was plus 3. In January, 1926, the spinal fluid Wassermann reaction was plus 4; the globulin was plus 2 and the cell count was 24. At this time the blood Wassermann reaction was negative. In August, 1927, the blood Wassermann reaction was plus 2; the spinal fluid Wassermann reaction was plus 3, the cell count 1, and globulin

tests and the colloidal gold curve were negative. Two blood Wassermann tests done in October were negative. A spinal fluid examination showed a negative Wassermann reaction, 3 cells, negative Pandy test and a colloidal gold curve of 0133200000. Electrical examination did not show any change from the normal. Roentgenograms of the upper dorsal and cervical spine showed slight marginal lipping due to osteo-arthritis.

The patient presented a typical history and typical symptoms of tabes dorsalis which involved the arms to a marked and the legs to a slight extent. In addition there was atrophy, weakness and fibrillary twitchings of the muscles of both shoulder girdles; these signs were more pronounced than one ordinarily encounters in this disease. Although opinions vary as to the exact circulation of the cord, Tilney and Riley made the statement that the ventromedian artery, a branch of the anterior spinal artery, supplied the anterior horn cells alone. I have assumed that in this case a thrombosis of that artery had occurred about the level of the fifth cervical segment and had produced the weakness, atrophy and fibrillary twitchings.

DISCUSSION

DR. T. H. WEISENBURG: The diagnosis of thrombosis of the anterior spinal artery in this case is clear. In making a diagnosis of thrombosis of any of the spinal cord arteries it is necessary to take into consideration the formation of the anterior spinal arteries. According to some authors the upper part of the anterior spinal artery has its origin from the vertebral and terminates at the level of the fifth cervical segment. The continuation of the anterior spinal artery below this part is made up from vessels which enter the cord laterally. It is obvious, therefore, that any thrombosis which occurs above the fifth cervical segment will give a different syndrome. It is also apparent that different syndromes can occur according to the location of the thrombosis.

In a previous meeting, at which cases of thrombosis of the anterior spinal artery in the thoracic and lumbar cord were shown from my clinic at the Infirmary for Nervous Diseases, some criticism was offered because in these cases the symptoms of degeneration of the lateral columns were not present. From a study of the supply of the anterior spinal artery it is obvious that the cells of the anterior horn receive their blood supply from this vessel, and that only occasionally does the supply extend to the lateral columns. Therefore the presence of symptoms of degeneration in the lateral columns cannot be expected in each instance of thrombosis of the anterior spinal artery.

DR. S. F. GILPIN: I am surprised that the diagnosis in this case is now tabes dorsalis. The history of onset of the illness is sudden, not at all like that in a case of tabes. While under my care I believed this was a case of syphilitic meningomyelitis of the cervical region, the neglect of treatment allowing time for organization of the gummatous exudate. As a result, the irritation of the posterior nerve roots accounted for the pain.

DR. M. A. BURNS: Will Dr. Michaels state whether, in taking the electrical reactions, there were definite reactions of degeneration? It seems that with the amount of atrophy and fibrillation there must be some involvement of the cells of the anterior horns.

DR. J. J. MICHAELS: Dr. Boyer tested the electrical reactions and reported that they did not show any change from the normal.

1. ISOLATED PARALYSIS OF THE SERRATUS MAGNUS.

2. LEAD PARALYSIS OF THE UPPER ARM TYPE. DR. CHARLES S. POTTS.

RHEUMATIC NODULES IN THE BRAIN. DR. N. W. WINKELMAN.

CLINICAL AND PATHOLOGICAL STUDY OF A CASE OF THROMBOSIS OF A SUPERIOR CEREBRAL VEIN. DR. RAYMOND W. WAGGONER.

These articles will be published in full in a later issue of the Archives.

A Pathologic State of the Choroid Plexuses in So-Called Essential Epilepsy. Dr. Alfred Gordon.

The case reported is that of a boy, aged 10, with epileptic convulsions. They were of generalized type and developed at the age of 5 following an obscure febrile state. Somatically, the case presented nothing worth mentioning. The vegetative and sensorimotor systems were intact; no localized abnormal symptoms were detected. The humors and excretions of the body did not show any abnormalities. There were no indications that the epileptic seizures had an organic basis. The patient died from bronchopneumonia. A complete necropsy revealed the only pathologic tissue in the choroid plexuses and in the ependyma of the anterior horns of the lateral ventricles. The plexuses appeared externally congested, thick, large, and hard under the fingers. Sections were stained with ammonia-carmine. The numerous glomeruli, which are held together by the delicate connective tissue stroma and which present a villous-like appearance, were seen with their cubic epithelial cells and blood vessels. The latter were filled with thrombi of all sizes and surrounded by a thickened external wall as the result of an inflammatory process which was evidently of long standing. The ependyma was thickened and the blood vessels also were filled with thrombi but not to the same extent.

The case shows that, in addition to gross lesions, the stimulating surface for convulsions may be localized not in the cortex but in a ventricular cavity, and even in areas far removed from the motor cortex.

Dervish Spasm in Encephalitis. Dr. Charles W. Burr.

This article will be published in another issue of the Archives.

Book Reviews

LES RAMOLLISSEMENTS SYLVIENS. By MAURICE LEVY. Price, 28 francs. Pp. 200. Paris: Gaston Doin Company, 1927.

A new point of view is expressed in this book with regard to cerebral localization, the arterial distribution being taken as the foundation. In reality it is a resuscitation of a view held by Charcot, and it represents one of the last pieces of work inspired by Charles Foix, whose description of the syndromes of the anterior and posterior cerebral arteries has become classic. Since cerebral lesions are so frequently vascular in origin, it is curious that clinical anatomy has not been more frequently approached from this aspect. Although the syndromes of the anterior and posterior cerebral arteries are fairly fixed, those of the sylvian artery are extremely numerous and often complex, depending as they do on variations not only in the artery itself with its branches, but also on the location of the obstruction. There are certain differences from case to case in the ramifications of the sylvian artery, the main features of which are described by the author on the basis of fifty brains examined. One can differentiate, however, the superficial and deep, the temporal and the ascending branches, since these give rise to the major syndromes. It is a fact, however, that the complete distribution of the artery is not always affected, the more distal parts as a rule being preserved better than the ones immediately beyond the location of the obstruction.

In deciding from the clinical aspects of the case whether the superficial or the deep branches are affected, the author believes that three signs favor deep softening: (*a*) the absence of hemianopia; (*b*) the absence of sensory disorder, and (*c*) the equality of the paralysis of the two limbs. When the lesion is in the left hemisphere the resultant aphasia more or less corresponds with Broca's type. In the case of hemiplegia with sensory disorders of a pronounced type one may expect to find softening in the distribution of the superficial branches; if the posterior branches are affected hemianopia is almost constant. With arterial occlusion in this area, the type of language disturbance runs more to the Wernicke form, with apraxia. The ascending branches of the sylvian artery supplying the third frontal and central convolutions are more apt to give rise, when obstructed, to localized paralysis, with considerable tendency toward recovery. When they occur on the left side, anarthria is the rule. There is a certain tendency to symmetry in softening of the brain and multiple foci are not at all uncommon, giving rise to pseudothalamic syndromes.

The author describes forty-five cases and gives in detail the clinical histories and the results of the pathologic examinations. The work is illustrated with good photographs and crude sketches; the plate taken from Schiff-Wertheimer is an excellent schema for topical vascular localization.

POSTENCEPHALITIC RESPIRATORY DISORDERS. REVIEW OF SYNDROME, CASE REPORTS, PHYSIOPATHOLOGY, PSYCHOPATHOLOGY AND THERAPY. By SMITH ELY JELLIFFE, M.D., PH.D. Monograph no. 45. Price, $2.50. Pp. 135. New York and Washington: Nervous and Mental Disease Publishing Company, 1927.

Much of the material in this monograph is already familiar to the readers of the ARCHIVES through the article on the phenomenology of postencephalitic respiratory disorders which appeared in the May, 1927, issue. In the book this material has been amplified and new matter added which concerns chiefly the facts secured from a psychoanalytic study of the patient in case 1. From the discussion of these facts, it is evident that the author regards the particular forms of respiratory disorder with which he is concerned as reactions occur-

ring from lower levels (in the sense of Hughlings Jackson) of the nervous system. As a result of the injury by the encephalitic virus the higher levels have been isolated; to use the terms of Freud, the patient has regressed from the ego more or less toward the id. The respiratory phenomena are, therefore, to be regarded as primitive forms of erotic gratification. One finds it difficult to understand how psychoanalysis can replace connections with higher brain levels that have been destroyed by disease, and the author frankly admits that many postencephalitic or chronic encephalitic manifestations are hopeless. The patient around whom the monograph is written, however, showed a remarkable recovery — he had not had respiratory spasms for eighteen months at the time of writing. The second patient used as a paradigm for the respiratory disorders under consideration had as yet not shown improvement. The material is an interesting contribution to the behavior value of respiratory disorders whether due to encephalitis or not. The literature is admirably reviewed. The discussion provides much food for thought concerning the sorting out of cases in which the situation is hopeless because of the destruction of nerve paths, from those in which psychoanalytic or other educational measures may bring results, though the author does not view them from this angle. The successful outcome in one case of this apparently hopeless nature certainly justifies the author in recommending the adoption of such measures. Undoubtedly, also, such studies will throw light on the significance of lower level or primitive types of reaction.

ZELLAUFBAU DER GROSSHIRNRINDE DES MENSCHEN. Zehn Vorlesungen, by DR. CONSTANTIN VON ECONOMO, Professor of Neurology and Psychiatry, University of Vienna. Paper, 146 pp., with 61 illustrations. Berlin: Julius Springer, 1927.

The ten lectures here presented have been delivered to the students of psychiatry in the University of Vienna since 1923. They have been printed with the purpose of presenting in handy form a brief outline of the cellular architectonics of the cortex. They are not intended to replace larger and more detailed accounts such as that by the author, in collaboration with Koskinas, which appeared in 1925, but rather to serve as an introduction to a more detailed study. The two first lectures are devoted to general considerations of the cellular structure of the cortex and are followed by two on the frontal lobe, two on the parietal, one each on the occipital and temporal lobes, and two on the gyrus cinguli. Though the space is limited, the material is simply and clearly presented and is thoroughly up to date; the illustrations and printing are excellent. The author is to be complimented on the manner in which he has supplied a long felt want. The book can be heartily recommended to all students of neurology who will owe one more debt of gratitude to its illustrious author.

MIKROSKOPISCH-TOPOGRAPHISCHER ATLAS DES MENSCHLICHEN ZENTALNERVENSYSTEMS. By PROF. DR. OTTO MARBURG. Vorstand des neurologischen Institutes der Wiener Universität. Leipzig und Wien, Franz Deuticke, 1927. Price 28 marks, bound, 33 marks. 200 pages, 40 illustrations and 32 original drawings. 3rd Edition.

The third edition of the well known microscopic anatomy of the central nervous system is new in every sense of the word. Its author, Obersteiner's successor in Vienna, needs little introduction to American students of neurology. In the first chapter, the spinal cord is thoroughly considered, and a careful description of the structure of sixteen different levels is given and not the customary four or five of the usual textbook. In the second chapter, the brain stem is described at twenty different levels. In this chapter the striatum and pallidum (the Vogt nomenclature is used) are placed and described. The

third chapter takes up the cerebrum. The illustrations in the main are excellent. The book is worth while and is strongly recommended to students of the nervous system.

NEUROLOGISCHE UNTERSUCHUNGS-SCHEMATA. By PROF. DR. FRANZ KRAMER. Price, RM. 4.80. Pp. 104. Berlin: Julius Springer, 1927.

This book consists of six original plates and models. The first two show the anterior and posterior views of the human body and give the electrical points of irritation for both nerves and muscles. The third and fourth plates show the peripheral nerve distribution, and the fifth and sixth the spinal root distribution. The third and fourth differ from similar plates used in most textbooks in that they are more diagrammatic and do not conform to the usual restricted outline that is given in such drawings to peripheral nerve distributions. The rest of the book contains outlines of the human body; these can be torn out and used for the record of sensory impressions.